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THE PREMATURE INFANT

A STUDY OF THE EFFECTS OF ATMOSPHERIC CONDITIONS ON GROWTH AND ON DEVELOPMENT

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INTRODUCTION [1]

Many years ago, Budin,[2] the French obstetrician, in a series of lectures to his students, emphasized the special needs of premature infants with reference to (*a*) temperature and chilling, (*b*) feeding and (*c*) the diseases to which they are especially susceptible. Since then, the subject has received well merited attention from numerous clinical investigators, but notwithstanding the advance in knowledge relating to this special group of infants, statisitcs show that 65 per cent of the fatalities within the first few weeks after birth occur in premature infants. Of course, a large number of deaths are beyond control because of immature structural development; yet, as Langstein [3] pointed out, "a great number of premature children die, not because their organs are too immature to stand the strain but because, partly through ignorance and partly for social reasons, offenses against care and nutrition are committed to which premature children only too readily succumb."

Successful rearing of premature infants depends primarily on four basic principles: (*a*) stabilization of body temperature, (*b*) adequate and proper nutriment, (*c*) prophylaxis against infection and (*d*) intelligent nursing and medical care. The stabilization of body temperature through accurate control of environmental conditions has been least adequately dealt with, and the present study consists of a further attempt to establish the factors of this important requirement. The problem demands accurate description of the interrelated effects of air temperature, humidity and ventilation rate on the heat-regulating mechanism of premature infants. Obviously a successful study implies control of these environmental variables. And this is rather elaborate. Most of the methods in vogue fall far short of an ideal air control on account of limited air space, inadequate ventilation, insufficient humidification in winter and lack of facilities for cooling and dehumidifying

1. The specially devised circumstances under which these studies have been conducted obviously do not necessitate a complete review of the voluminous literature respecting prematurity. For a more comprehensive consideration of the literature dealing with the premature infant, attention is directed to the writings of Hess (Premature and Congenitally Diseased Infants, Philadelphia, Lea & Febiger, 1922), Yllpö (in Langstein, Leo: Beitrag zur Physiologie, Pathologie und sozialen Hygiene des Kindesalters, Berlin, Julius Springer, 1919) and Talbot and his co-workers (Basal Metabolism in Relation to Body Surface at Different Ages with Special Reference to Prematurity, Proc. Soc. Exper. Biol. & Med. **19**:309, 1922; The Basal Metabolism of Prematurity: II. Relation of Basal Metabolism to Caloric Intake and Weight Curve, Am. J. Dis. Child. **24**:95 [Aug.] 1922; III. Metabolism Findings in Twenty-One Premature Infants, ibid. **26**:29 [July] 1923; Skin Temperatures of Children, ibid. **42**:965 [Oct.] 1931).

2. Budin, Pierre: Le nourrisson; alimentation et hygiène; enfants débiles, enfants nés à terme; leçons cliniques, Paris, O. Doin, 1900.

3. Langstein, Leo, quoted by Steinforth, T.: Das Schicksal frühgeborenen Kinder, Zentralbl. f. Gynäk. **52**:1332 (May 26) 1928.

the air in warm weather. In instances in which mechanical ventilation has been used, there has been a tendency to fix the temperature of a single room at or about 80 F., but without special regard to the requirements of the individual infants. Humidification by means of steam humidifiers, pans of hot water or mechanical atomizing devices inside the rooms and dehumidification in warm weather by means of calcium chloride have proved quite ineffectual.

In addition to stabilization of body temperature through accurate control of environmental variables, the question naturally arises as to whether the rate of growth and the mortality rate would be affected favorably in an environment in which the interrelated air conditions (ventilation, temperature and humidity) were properly adjusted and accurately controlled.

PLAN OF STUDY

To investigate these problems, a complete central air-conditioning system was installed whereby the temperature, humidity and ventilation in the nurseries for premature infants could be maintained at any desired level, regardless of weather. Hereafter the improved nurseries will be referred to as "conditioned nurseries" to distinguish them from the old "unconditioned" nursery which did not possess this advantage.

With the definite objective of reducing to a minimum those influences which would obviously enter into the drawing of valid conclusions, special consideration was given to keeping uniform such variables as (*a*) the type of subject, (*b*) hygiene and clothing, (*c*) nutriment and (*d*) medical and nursing care. The following routine was adhered to as closely as was feasible without detriment to the patients.

Observations were made on three groups of patients: (*a*) normal premature infants of a fetal age between 6 and 9 months, approximately, weighing from 1½ to 5 pounds and admitted to the hospital from a few hours to several weeks after birth; (*b*) congenitally diseased premature infants or those suffering from congenital anomalies and from other pathologic conditions incident to immature birth, and (*c*) premature infants with acute and chronic infections and infants dying within forty-eight hours after admission.

At the time of admission, and during their stay in the conditioned nurseries, the infants were clothed in a uniform manner and kept in a basinet with uniform external coverings. The clothing consisted of a silk and wool shirt, a diaper and either an eiderdown jacket or a cotton flannel nightgown. Only in special cases was a knitted bonnet used. The bed was made in the usual fashion with a cotton bottom sheet, head towel and a top covering of cotton sheet, blanket and spread. Very small infants were covered with a woolen blanket and placed between light weight blankets instead of sheets.

Fixed air conditions of the nurseries were relied on to regulate the body temperature, with the exception of the first few hours or days after admission when certain infants needed additional heat. Oil baths were given every other day as a routine measure until the infants reached a weight of 4 pounds, after which they received baths of warm water and soap. All infants were weighed soon after reaching the nursery and twice a week thereafter. The body length was measured at regular intervals (on admission, weekly and at the time of discharge). The rectal temperature was recorded every four hours, except when more frequent readings were desired.

A standardized plan was followed with respect to the type of food, the number of calories per pound of body weight and the interval and mode of feeding. Either one of two formulas, each containing about 20 calories per ounce, was used. Pooled woman's milk with at least 3 per cent fat was given most frequently, but when this was not available a modified formula consisting of 17 ounces of cow's milk (2 per cent fat) and 3 ounces of 50 per cent solution of Karo syrup was substituted. The amount of food was governed somewhat by the age and weight of the infant, but the average daily caloric value did not exceed 60 calories per pound. Antirachitic and antiscorbutic agents (cod liver oil, haliver oil, viosterol and orange juice) were not administered, as a rule, until the infants weighed at least 4 pounds, or in the case of very small infants who had to remain in the nursery over two months. The feeding interval was set at three hours (eight feedings), to be increased to four hours (six feedings) according to the weight and activity of the patient. To patients in whom the sucking reflex was absent, food was given by gavage. The rubber tube was passed into the upper part of the esophagus 4 inches from the lips. The direct introduction of food into the stomach was discouraged. With the development of the sucking reflex, as indicated by sucking movements on the gavage tube, and signs of increased physical activity, feeding by gavage was replaced by the Breck feeder. Thereafter, food was given in the regulation manner from a bottle with a nipple.

Every care was taken to guard against the spread of infections by direct or indirect contact. New patients in whom severe acute or chronic infections were detected were treated in a special nursery or inside a Hess bed in the general wards. Likewise, doctors, nurses and other personnel of the hospital who showed clinical signs of disease were not permitted to come in contact with the patients.

For the purpose of securing comparative data, the hospital records of the premature infants treated over a period of three years in the unconditioned nursery (1923 to 1925, inclusive) were analyzed. It is obvious that the data are not directly comparable with those obtained from 1926 to 1929, since in the former years a uniform plan of care

was not followed. Nevertheless, by contrast the data serve to illustrate the beneficial effects of air conditions maintained automatically at fixed levels.

A trained technician transferred essential data[4] from the hospital records of each patient to a special record sheet, each week. Thereby it was possible to check the progress at different intervals and to introduce new or additional methods of approach to the subject from time to time. Also, the compilation of the data in this way simplified the arduous task of analyzing, statistically, the information from which the conclusions were drawn.

DESCRIPTION OF THE AIR-CONDITIONED NURSERIES

General Specifications. — The nurseries consist of three separate rooms with the following dimensions: 12 by 8 by 12 feet; 12 by 12 by 12 feet, and 11 feet, 9 inches by 20 by 9 feet, the last dimension being the height in each instance. All three rooms are equipped with double windows. The first two rooms are reserved exclusively for premature infants and together they accommodate twelve infants (fig. 1). The third room, which accommodates from twelve to sixteen infants, is used as an observation nursery for special types of cases. One of the larger rooms was partitioned into cubicles at the time the system was installed, but the partitions were removed a few years later.

The mechanical equipment,[5] which was placed in the basement of the building, has sufficient capacity to produce about twenty-five changes of air an hour in each of the three rooms. This high rate was found to be necessary in order to keep the atmosphere free from odors and in order to control adequately the temperature and humidity in the extreme weather of this locality. By proper distribution of air, drafts were avoided. The movement of air about the beds was about 15 feet a minute.

It is possible to adjust the apparatus so that wide ranges in the air conditions can be secured. In winter, each of the three rooms may be kept at a maximum temperature of 110 F. with a maximum absolute humidity of about 220 grains of moisture per pound of air, when all the air is taken from outdoors at 0 F. In hot weather, the rooms

4. The units of measurement employed in this study are as follows: for body weight, the pound (0.455 Kg., approximately); for body length, the inch (2.54 cm.); for temperature, the Fahrenheit scale (C. = 5/9 F. —32); for food energy, the kilogram calory (large calory).

5. A more detailed description of the engineering aspects of this air-conditioning installation has appeared elsewhere. Yaglou, C. P.; Drinker, P., and Blackfan, K. D.: Application of Air-Conditioning to Premature Nurseries in Hospitals, J. Am. Soc. Heat. & Ventilat. Eng. (Sect. Heat., Pip. & Air-Condit.) **2**:605, 1930.

can be cooled to a temperature of 75 F. and the absolute humidity lowered to 70 grains per pound of air. In cool weather, lower indoor temperatures are possible and, by recirculating part of the air, the temperature and humidity can be kept at a still lower level. Any desired air condition within the specified range can be maintained automatically in summer or winter regardless of outdoor weather.

Description of Apparatus.—A simple diagram of the central air-conditioning apparatus is shown in figure 2 and a photograph of it in figure 3. The essential principles of operation are as follows: Air from outdoors, drawn in by fan suction, passes over the preheaters (on the left of figure 2) which automatically raise its temperature to

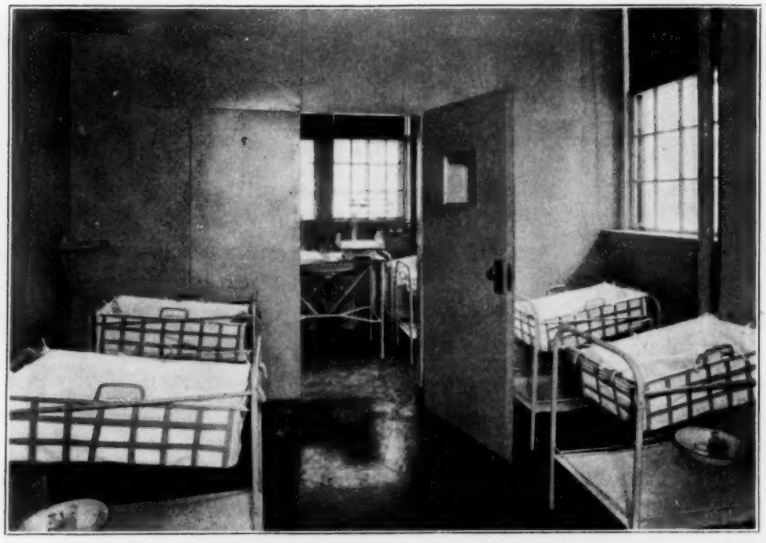

Fig. 1.—Nursery for premature infants showing the outer room and inner room, separated by a metal partition and a heavy metal door opening into the outer ward. There is space for six infants in each ward.

about 45 F., thus preventing the water from freezing in cold weather. The air then passes through the spray chamber, where it comes in contact with a finely atomized mist of water emerging under pressure from the nozzles of the spray. A centrifugal water pump (not shown in figure 2) maintains the circulation through the spray system. This procedure washes out the coarse dust in the air and removes soluble impurities. At the same time, the air absorbs or gives up moisture, according to the temperature of the water. In this way, the humidity in the rooms is regulated. Drops of water and dust carried over by the air stream from the spray chamber are caught by impingement against the eliminator plates (on the right of figure 2). The fan then

forces the air over individual heaters, two stacks for each room, and thence into the rooms. The conditioned air enters the rooms near the ceiling and, after circulating across the room, is withdrawn near the

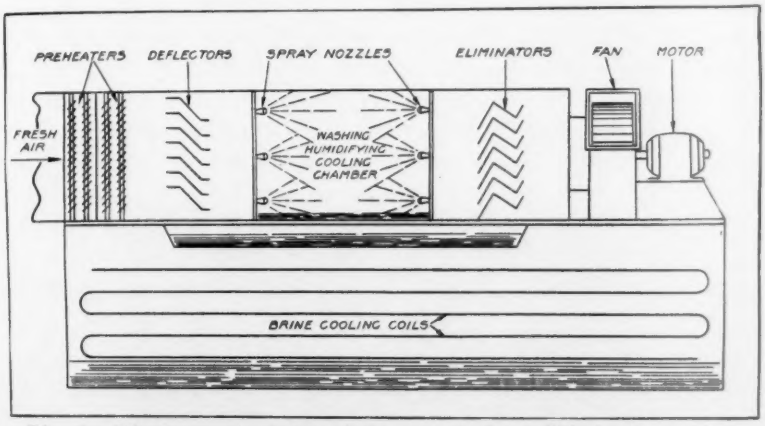

Fig. 2.—Diagrammatic sketch of the central air-conditioning apparatus.

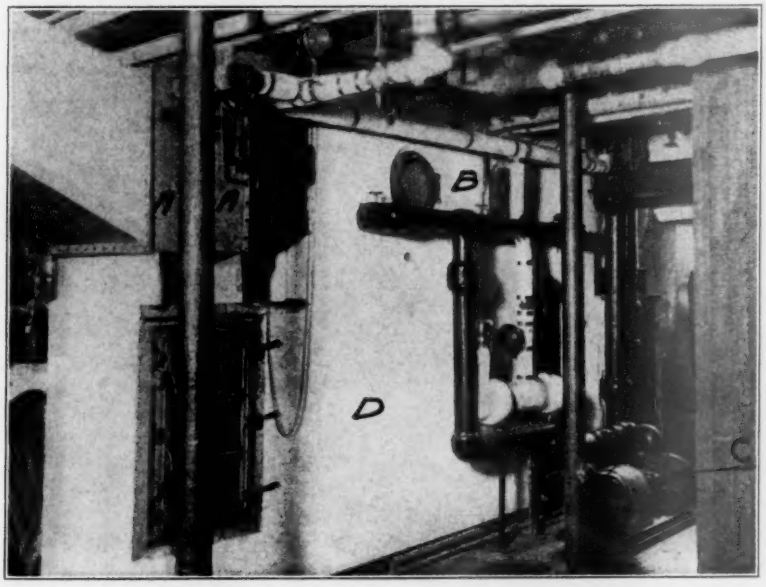

Fig. 3.—Central air-conditioning apparatus situated in the basement directly under the nursery: *A*, preheaters; *B*, spray chambers; *C*, water pump, and *D*, water cooler.

floor by means of an exhaust fan. Figure 4 shows the general arrangement of supply and exhaust ducts in the larger of the two rooms reserved for the premature infants. The used air may be expelled

outdoors, or part of it may be returned to the central apparatus for reconditioning and recirculation.

In winter the dry bulb temperature in the rooms is regulated automatically by means of thermostats which control the flow of steam through the individual indirect heaters. The humidity is regulated at the central apparatus by controlling the temperature of the water. A heater warms the water on its way to the sprays. A thermostat at the exit of the air washer controls the amount of steam flowing through the water heater, so as to maintain automatically a dew point of about

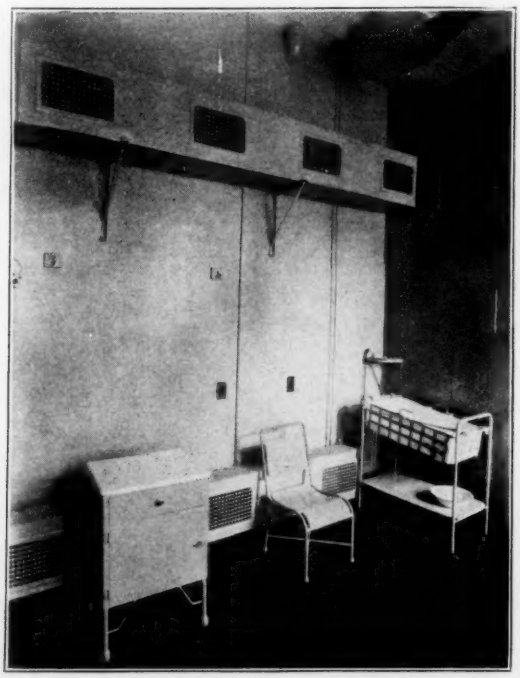

Fig. 4.—Supply (top) and exhaust (bottom) ducts in larger nursery for premature infants.

64 F. in the air leaving the air washer. This corresponds to a relative humidity of 65 per cent when the temperature of the room is 77 F. With higher temperatures, the relative humidity would be less, and vice versa, since with a single air washer the dew point, or moisture content, in all rooms has to be the same.

In summer, the warm and humid air from outdoors is cooled and dehumidified to 64 F. by contact with the spray of cold water. The water is cooled in the lower chamber of the apparatus (fig. 2) by trickling over cold pipes through which brine is circulated under pressure. The thermostat at the exit of the air washer is made to control

the flow of brine through the cooling pipes so as to maintain the desired dew point of 64 F. In passing through the fan and ducts the temperature of the air increases from 2 to 7 F., depending on the location of the room and on the weather conditions. In circulating through the rooms, the air absorbs sufficient heat from the warm walls, glass, lights and bodies of occupants to raise its temperature and at the same time to decrease the relative humidity to the desired degree. If the leakage of heat into the rooms through the walls and glass is not sufficient to produce this effect, as is often the case in cool weather, the reheaters automatically furnish whatever additional heat is needed.

Continuous permanent records of dry and wet bulb temperatures in the rooms are made by means of automatic recorders.

Success in applying these systems to nurseries for premature infants depends as much on operation as on design. The operation of the equipment, therefore, should not be entrusted solely to the engineer at the hospital unless he understands well the principles of air conditioning. The system should be thoroughly checked once or twice every year, and care should be taken to keep the apparatus clean, for if mud and fungi are allowed to accumulate in the air washer and Baudelot cooler, musty and sour odors will pollute the air in the rooms.

PHYSIOLOGIC RESPONSES TO HEAT AND COLD

Experience has shown that the heat-regulatory mechanism of premature infants is not fully developed at the time of birth, and that unless the infants are kept warm by the application of external heat, the body temperature gradually falls; in some instances it fails to rise again, with detrimental or fatal consequences. The inability of the premature infant to regulate and maintain a normal body temperature is attributed largely to incomplete development of the nervous system, as a result of which there is an imperfect balance between loss of heat and production of heat.

Hypothermia in premature infants is the result of an excess in loss of heat over production of heat. As Talbot and his co-workers [6] said:

> Their heat production is very low after birth and on the expected birthday the total heat production is still less than that of the average infant born at term. Among the factors which favor lowering of the body temperature in the prematurely born infant are the relatively great area of the heat-eliminating surface, i. e., the skin, as compared with body weight, the lack of subcutaneous fat which favors escape of heat from the more vital tissues of the body, the normally low

6. Talbot, F. B.; Sisson, W. R.; Moriarty, M. E., and Dalrymple, A. J.: The Basal Metabolism of Prematurity: III. Metabolism Findings in Twenty-One Premature Infants, Am. J. Dis. Child. **26**:29 (July) 1923. Talbot, F. B.; Bates, V.; Bates, E., and Dalrymple, A. J.: Skin Temperature of Children, ibid. **42**:965 (Oct.) 1931.

production of heat by the organism itself, and the failure to increase this production by shivering, crying and other forms of exercise when the environmental temperature falls below that optimal for the child. In hyperthermia, or when the heat production increases, there is no corresponding increase in the elimination of excess heat. The sweat glands do not function as efficiently as they do in the fully developed or "mature" new-born infant, and sometimes they do not act at all.

Observations on the response to heat and cold were made in the air-conditioned nurseries under accurately controlled environments. Altogether sixteen infants were chosen; three full-term normal infants for controls and thirteen premature infants of various fetal ages, chronological ages and body weights (table 1). Both normal and congenitally diseased premature infants were included in the investigation. The full-term infants were brought into the conditioned nurseries at least two hours before the observations were begun in order to give them an opportunity to adapt themselves to the particular air conditions in the nursery.

The temperature of the room, in one series of observations, was increased from the customary initial level between 77 and 80 F. to approximately 100 F. In another series of observations the temperature was lowered from the same initial level to approximately 63 F. The relative humidity in both series averaged about 50 per cent. Other conditions were kept unaltered. These extremes in temperature are representative of the maximum and minimum seasonal variations in temperature to which the infants were sometimes exposed in the unconditioned nursery prior to the installation of mechanical apparatus.

The response of the infants to environmental conditions was determined by observing changes in the skin and in the rectal temperature, vasomotor variations and other reactions, such as redness, sweating, restlessness, cyanosis, crying and shivering. The rectal and skin temperatures were recorded at frequent intervals by the thermo-electric method which has been described by Benedict.[7] Preliminary readings of the skin temperature were taken on seventeen different areas, but subsequently only the temperature of the right cheek was recorded, as it was found that the temperature at this point was representative of the seventeen areas, as fixed by Talbot.[8] The pulse rate varied so widely that it was not recorded regularly.

In table 1 is shown the physiologic response of the patients to heat and cold. The changes in rectal and skin temperatures are those taken one, two, three and three and one-half hours after changing the temperature of the air. The data reveal a considerable individual varia-

7. Benedict, F. G.; Miles, W. R., and Johnson, Alice: The Temperature of the Human Skin, Proc. Nat. Acad. Sc. **5**:218, 1919.

8. Talbot, F. B.; Dalrymple, A. J., and Hendry, M. F.: Skin Temperatures in Normal Children, Am. J. Dis. Child. **30**:483 (Oct.) 1925.

tion in the reactions to heat and cold, especially among the congenitally diseased premature infants. In the normal premature infants the physiologic response and the time of recovery from the effects of heat and cold appear to be related to the degree of immaturity. This is brought out clearly in figures 5 and 6, which show observations on three infants before, during and after exposure to heat and cold. In these figures, the reactions of a full-term normal infant are compared with those of two apparently normal premature infants of different fetal ages and body weights.

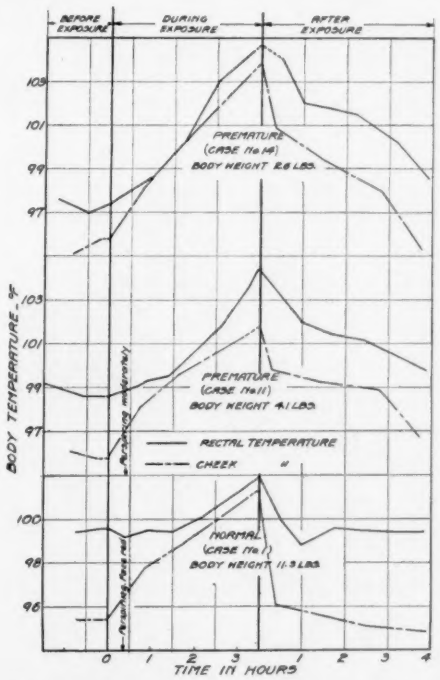
BEFORE EXPOSURE
DURING EXPOSURE
AFTER EXPOSURE
PREMATURE (CASE No 14) BODY WEIGHT 2.6 LBS.
PREMATURE (CASE No 11) BODY WEIGHT 4.1 LBS.
RECTAL TEMPERATURE
CHEEK "
NORMAL (CASE No 1) BODY WEIGHT 11.3 LBS.
BODY TEMPERATURE °F.
TIME IN HOURS

Fig. 5.—Effect of raising the temperature of the room from about 80 F. to 100 F.

It will be observed that at an environmental temperature of 100 F. the rectal temperature of normal infant 1 did not rise for about one and one-half hours, despite the marked rise in cheek temperature. During the same period of time the rectal temperature of premature infant 11 rose 1 F., and that of premature infant 14 rose about 2 F. At the end of three and one-half hours the total rise in the rectal temperature of the full-term infant was 2.3 F., as compared with 5.8 and 7.3 F. for premature infants 11 and 14, respectively. In the normal infant, the rise in cheek temperature after three and one-half hours was 5.9 F., while in the premature infants it was 6 and 8 F., respectively.

TABLE 1.—*Physiologic Response to Heat and Cold*

Classification According to Body Weight				100 F.; Heat 50% Relative Humidity										63 F.; Cold 50% Relative Humidity									
				Increase in Body Temperatures at End of Specified Periods of Exposure, F.								Difference Between Rectal and Cheek Temperature When Perspiration Began	Time to Regain Initial Body Temperature in Hours		Decrease in Body Temperatures at End of Specified Periods of Exposure, F.							Time to Regain Initial Body Temperature in Hours	
				1 Hour		2 Hours		3 Hours		3½ Hours					1 Hour		2 Hours		3 Hours		3½ Hours		
Case	Age, Wks.	Body Weight Lbs.	Body Weight Oz.	Rectal	Cheek	Rectal	Cheek	Rectal	Cheek	Rectal	Cheek			Comment	Rectal	Cheek	Rectal	Cheek	Rectal	Cheek	Rectal	Cheek		Comment
Normal Controls—																							
1	11	11	5	—0.1	2.6	0.3	3.9	1.6	5.2	2.2	5.8	2.8	1	Perspiring freely; face red; crying									
2	5	7	4	0.0	5.2	0.5	7.6	...	...	...	...	4.5	.....	Perspiring freely; face red; hands and feet clammy; quiet	+0.8	2.8	+0.3	2.0	0.0	3.2	0.3	4.0	.....	Cried at first; restless thereafter; skin pale
3	3	5	14	0.0	2.8	0.0	3.6	...	...	...	...	4.0	.....	Perspiring freely; face red; hands and feet clammy; quiet	0.0	0.8	0.3	2.8	0.1	4.6	0.3	4.8	.....	Quiet; whimpering occasionally
Congenitally Diseased and Normal Premature Infants—																							
4	8	5	7	0.0	4.7	0.5	6.0	...	...	...	...	4.2	.....	Perspiring freely; face red; went to sleep	+0.1	1.1	0.7	3.3	0.1	3.1	0.4	4.8	.....	Quiet; face slightly blue
5	18	5	5	0.2	4.1	0.0	6.4	...	...	...	...	2.8	.....	Slight perspiration; quiet	0.0	5.3	0.5	7.3	0.4	9.1	0.4	10.1	.....	Hands and feet cold and blue; cried a little
6	10	5	4	0.7	3.2	1.9	4.2	2.9	5.1	3.0	5.5	2.8	1¼	Moderate perspiration; face red	0.7	1.8	1.8	2.3	1.3	3.1	0.9	3.4	1½	Cried at first

7	7	4	14	1.0	4.3	1.2	4.9	2.3	5.3	2.6	5.5	1.4	1	Moderate perspiration; face red; quiet	0.7	2.9	1.3	2.9	1.7	3.3	1.7	3.5	Over 3	Cried at first; face slightly blue
8	11	4	11	0.7	3.5	1.7	4.7	4.2	6.0	5.2	6.6	3.1	2½	Slight perspiration; face red; quiet	0.7	1.9	1.2	2.7	1.6	3.0	1.4	3.2	3	Cried hard
9	11	4	9	2.0	4.0	3.3	6.1	6.2	9.2	7.1	10.6	3.5	Over 4	Slight perspiration; face and hands red; cried a little	+0.2	2.1	0.5	2.4	0.9	2.8	0.8	3.0	Over 3	Cried at first
10	3	4	3	0.7	5.7	0.0	6.2	...	...	...	...	3.8	.....	Moderate perspiration; face red; quiet throughout	0.7	1.9	1.9	4.1	...	...	...	...	.....	Quiet; hands very blue; removed to warmer room
11	9	4	2	0.8	2.8	2.1	4.3	4.4	5.4	5.8	6.0	1.8	Over 4	Moderate perspiration; face red; quiet throughout	0.6	1.7	1.7	2.5	1.0	2.5	1.0	2.4	3	Slightly active
12	4	4	0	1.4	3.8	3.8	6.1	6.6	7.6	7.6	8.3	0.8	Over 4	Slight perspiration; face pink										
13	5	3	12	1.2	2.5	3.9	4.1	4.8	5.4	5.5	6.2	1.1	Over 4	Slight perspiration; face red; quiet	0.5	1.7	1.1	2.9	1.7	6.1	1.8	7.3	.....	Cried hard; face and hands blue; removed to warmer room
14	1½	2	10	1.2	2.8	3.8	5.0	6.5	7.1	7.3	8.1	No perspiration	Over 4	Did not perspire; face slightly pink	2.1	2.6	...	...	...	...	...	...	.....	Inactive; removed to warmer room; face and hands blue
15	2 da	1	14	0.5	+6.1	1.7	7.7	1.8	7.4	...	...	1.0	.....	Trace of perspiration; quiet										
16	5 da.	1	6	−1.0	6.7	0.3	10.1	0.1	7.7	...	...	No perspiration	.....	Did not perspire; skin blue and yellow over entire body										

The cheek and rectal temperatures of the full-term infant returned to their normal level in about one and one-half hours, whereas it took more than three hours for the cheek and rectal temperatures of the premature infants to regain their initial level.

All three infants showed protective reflexes, such as reddening of the skin and other vasomotor reactions. The normal full-term infant commenced to perspire when the difference in temperature between the rectum and the cheek was about 2.8 F. (fig. 5). He perspired freely. Premature infant 11 did not begin to perspire until this difference in

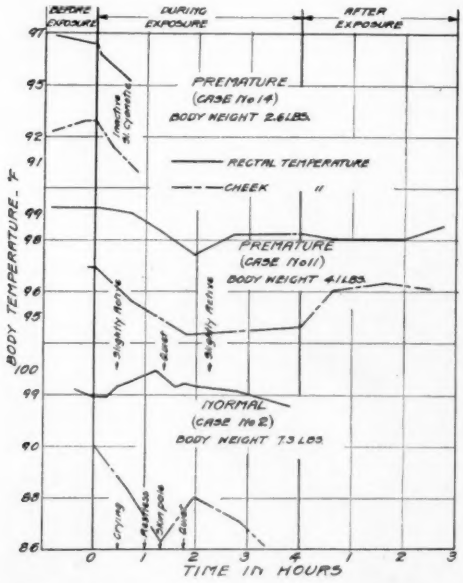
BEFORE EXPOSURE
DURING EXPOSURE
AFTER EXPOSURE
PREMATURE (CASE No 14) BODY WEIGHT 2.6 LBS.
RECTAL TEMPERATURE
CHEEK "
PREMATURE (CASE No 11) BODY WEIGHT 4 LBS.
NORMAL (CASE No 2) BODY WEIGHT 7.3 LBS.
BODY TEMPERATURE - F.
TIME IN HOURS

Fig. 6.—Effect of lowering the temperature of the room from about 80 F. to 63 F.

temperature reached 1.9 F., and the extent of perspiration was less than that of the normal infant. Premature infant 14 did not perspire.

The responses of the three infants to lower temperature is shown graphically in figure 6. Soon after the temperature was lowered, normal infant 1 exhibited definite defense reactions, such as crying, restlessness and pallor of the skin. In spite of a steep drop in cheek temperature, the rectal temperature rose to a maximum of 1 F., and for about three hours it remained at a level appreciably higher than the initial rectal temperature. Between the third and the fourth hours there was a slight drop, and near the end of the fourth hour the rectal temperature was only 0.4 F. below its initial level. The pulse rate rose with the rectal temperature from about 136 to a maximum

of 168 beats per minute, after which it began to decline gradually, falling to 128 beats per minute near the end of the fourth hour.

The foregoing reactions, so far as general tendencies are concerned, are similar to those observed in healthy adults. In these subjects compensation for increased loss of body heat is effected by increased metabolism, through shivering or otherwise, and by decreased peripheral circulation. The surface blood vessels become constricted and shrink farther below the surface, thus increasing the thickness of the insulating medium. The rectal temperature often rises on exposure to cold. The blood pressure increases, but the pulse rate and surface temperature decrease.

The reactions of the two premature infants to lowered temperature were somewhat different from those of the full-term infant. The rectal temperature of premature infant 11 did not rise as in the case of the full-term infant, but fell gradually with the fall in the cheek temperature (fig. 6). After two and one-half hours a new equilibrium was established at a body temperature level of about 1 F. lower than the initial level. After raising the temperature of the room to the original level (78 F.), the initial body temperature was not regained over the three hour period during which the observations were noted.

Premature infant 14 was removed to a warmer room after an exposure of fifty minutes because he became slightly cyanotic and inactive. In the first half hour the rectal temperature fell 1.2 F., as compared with the fall of 0.1 F. in premature infant 11 and with the rise of 0.4 F. in the full-term infant. Part of this fall in temperature was due, doubtless, to the fact that the normal environmental temperature required for premature infant 14 was higher than that for the other two infants. In other words, the contrast in temperature was somewhat greater for premature infant 14 than for premature infant 11 and normal infant 2.

Generally speaking, the infants in this study, as shown in table 1, exhibited more or less similar tendencies. With the exception of the smallest premature infant (16), the infants exhibited typical vasomotor reactions and other protective responses against heat and cold; however, the intensity of these reactions varied inversely as the body weight and fetal age. In all infants the cheek temperature varied considerably more than the rectal temperature and was quite irregular. Similar irregularities have been reported by Shelble [9] and Mendelssohn.[10]

9. Schelble, H.: Ueber Stamm- und Hauttemperaturen bei Säuglingen, Ztschr. f. Kinderh. **2**:62, 1911.

10. Mendelssohn, A.: Ueber das Wärmeregulationsvermögen des Säuglings, Ztschr. f. Kinderh. **5**:269, 1913.

The manner in which the two smallest infants (15 and 16) responded to a change in environmental temperature from 95 (plus two hot water bottles) to 100 F. is most interesting. In spite of the small difference in the environmental temperature, both infants showed a very steep rise in cheek temperature, while the rectal temperature changed little, especially in comparison with the reaction of the older and larger infants.

In summary, it may be said that in premature infants the physiologic response to, and the time of recovery from, the effects of heat and cold are related to the body weight and fetal age. In other words, the heat-regulatory mechanism is not so well developed as in normal full-term infants.

The heat-regulatory mechanism in full-term infants was adequate to protect them against excessive heat by vasomotor shifts of blood to the peripheral vessels and by an ample excretion of sweat. Sweating commenced when the difference in temperature between the skin and the rectum was from 2.8 to 4.5 F. In cold environments the regulation of the body temperature was equally effective. It was brought about by vasomotor shifts of blood to the internal organs concomitant with crying and restlessness.

In premature infants weighing between 4 and 5½ pounds, these protective responses were less marked than in the full-term infants, suggesting that the heat-regulatory power was inadequate. The rectal and cheek temperatures increased much more than in the full-term infants, and the difference in temperature between the cheek and the rectum at which perspiration began was smaller, varying within the limits of 0.8 and 4.2 F.

Premature infants weighing between 1½ and 4 pounds showed still less ability to regulate body temperature. Two of the four infants (13 and 15) in this group perspired slightly when the difference in temperature between the skin and the rectum approached 1 F. The other two infants did not perspire (14 and 16), and in infant 14 the reaction to cold after fifty minutes was so intense as to necessitate removal to a warmer environment.

These observations support the prevailing opinion concerning heat regulation in premature infants, thereby failing to confirm the controversial views advanced by Eckstein,[11] who concluded, from observations of body temperature in cool and warm baths, that the premature infant is not to any great measure thermolabile. The data herein recorded are in accord with the observations of Eross[12] and Meyer-

11. Eckstein, A.: Ueber die Wärmeregulierung der Frühgeburten, Ztschr. f. Kinderh. **42**:5, 1926.

12. Eross, Julius: Untersuchungen über die normalen Temperatur-Verhältnisse der Neugeborenen in den ersten 8 Lebenstagen, Jahrb. f. Kinderh. **24**:189, 1886.

stein,[13] who employed more extreme bath temperatures than Eckstein, and of Talbot,[14] who concluded that "the temperature of the skin as well as the body is affected directly by the surrounding temperature."

DETERMINATION OF OPTIMUM AIR CONDITIONS

It is now well recognized that the essential factor in determining the fitness of air, in the absence of any specific contaminating source (harmful dusts, gases and disease-producing organisms), is the maintenance of the physical condition of the air which favors the normal loss of body heat with the minimum strain on the part of the heat-regulating mechanism of the body. By the physical condition of the air is meant its temperature, humidity and rate of movement, which must be kept within proper limits in order to maintain the physiologic integrity of the internal environment of the organism.

While no single instrument has yet been devised to indicate the warmth or comfort of a given atmospheric condition, extensive investigations [15] carried out jointly by the United States Bureau of Mines, the United States Public Health Service and the Research Laboratory of the American Society of Heating and Ventilating Engineers resulted in the development of a single index—the so-called "effective temperature scale"—which expresses in one term the three factors concerned in loss of heat. This index was developed by estimating comparable air conditions by the effect produced on sensation of warmth and by the physiologic response of normal adults.

Within the effective temperature scale, a comfort zone has been established,[16] thus fixing various combinations of temperature, humidity and air movement giving uniform sensations of comfort. Under the air conditions defined by the comfort zone, the body was able to maintain thermal equilibrium with its environment, with the least conscious sensation to the subject, or with the minimum physiologic demand on the heat-regulating mechanism. On the other hand, air conditions outside the comfort zone were found to affect body temperature, pulse rate and blood pressure, and the metabolic rate was definitely increased on exposure to cold and warm environments.

It is, perhaps, unnecessary to point out here that neither the effective temperature index nor the comfort zone determined for adults has been found to hold in the case of premature infants, in whom the

13. Meyerstein, A.: Heise Bader als Test der Konstitution, Arch. f. Kinderh. **70**:88, 1922.

14. Talbot, F. B.: Skin Temperatures of Children, Am. J. Dis. Child. **42**:965 (Oct.) 1931.

15. Yaglou, C. P.: The Thermal Index of Atmospheric Conditions and Its Application to Sedentary and to Industrial Life, J. Indust. Hyg. **8**:5 (Sept.) 1926.

16. Engineer's Guide (Am. Soc. Heat. & Vent. Engineers) **11**:323, 1933.

metabolic and circulatory functions, as well as the development of other physiologic processes, are still more or less subnormal.

In order to determine the optimum environmental temperature and humidity for various groups of premature infants, different fixed percentages of relative humidity were maintained in the nurseries by means of the air-conditioning system, and the dry bulb temperature was adjusted by trial to the level needed to stabilize the body temperature. At first, relative humidities of 20 and 80 per cent were tried, but later they were changed to 30 and 65 per cent, as it was found that relative humidities above 65 per cent were distressing to the attendants, and symptoms of dehydration frequently occurred in premature infants when the humidity was kept below 30 per cent over a considerable period.

It was found that, other things being equal, the environmental temperature requirements depended to a considerable extent on the humidity of the air. When the humidity was fixed, the temperature requirements varied according to the weight and the constitutional state of the infants. With few exceptions (usually during the first few days after admission) the variation depended more on weight than on any other single factor (table 2). This was ascertained by correlating the environmental temperature requirements, average body temperature and fluctuation in body temperature with weight, age and length. The most significant relationships found were those with weight, in which case the deviations of the individual observations from the general trend were considerably smaller when plotted against weight than when plotted against either age or length. This is in accord with our findings on the physiologic response to heat and cold (p. 1183), and, as will be shown later, with the growth in weight and length (p. 1200), the incidence of digestive syndromes (p. 1211) and the mortality trend (p. 1220).

Therefore, in the first year of the study, the normal and the congenitally diseased premature infants were divided into subgroups and assigned to one or the other conditioned nursery, according to body weight. Normal premature infants weighing between 2 and 3 pounds were placed in the smaller nursery with an environmental temperature varying from 80 to 87 F., while infants weighing from 3 to 5 pounds were placed in the larger nursery with an environmental temperature varying from 75 to 80 F. With few exceptions, infants weighing more than 5 pounds were assigned to the general wards. Premature infants suffering from congenital anomalies or pathologic conditions incident to immature birth, owing to the greater range in their temperature requirements, were cared for in an electric incubator or heated beds inside the larger nursery. The smaller infants in this group often required, temporarily, temperatures as high as from 90 to 100 F.

Subsequently, a more detailed study of the effects of high and low humidity in stabilizing the body temperature was made by changing the environment in the nursery from high to low humidity alternately for a week at a time, making, during the first few weeks, whatever adjustments were necessary in the temperature of the room. Careful observations were made of gain in weight, incidence of diarrhea, vomiting, infection, mortality and general behavior of the infants under the two conditions of humidity. Thus, by studying the effects of the various combinations of temperature and humidity over long periods, we were able to determine the basic or average requirements for the various groups according to weight and constitutional state.

With a relative humidity of 65 per cent, the air temperature required to maintain equilibrium of body heat in the group of infants weighing from 3 to 5 pounds was found to be about 77 F. When the relative humidity was reduced to 30 per cent, however, it was necessary to increase the temperature to 80 F. Alternate exposures to each of these two air conditions for a week at a time resulted in no significant difference in the stabilization of body temperature.

But in prolonged exposures to relative low humidity, marked differences developed. Whenever the low humidity prevailed for two weeks or longer, the incidence of diarrhea was found to increase, body temperature became less stable, gains in weight were generally reduced and fatalities increased. In the majority of the affected infants, diarrhea was accompanied by, and in some cases followed by, fever and vomiting. This aspect of the situation will be discussed more fully. Continuous exposure to high humidity, on the other hand, gave satisfactory results. The effects of intermediate humidities were studied, but a relative humidity of 65 per cent was found to be more advantageous than any of the other values tried. Presumably the optimum humidity for premature infants may be higher than 65 per cent; but we have taken this value as the upper limit which is practicable and have adopted it as a standard.

In connection with the recommendation of 65 per cent relative humidity, it is important to emphasize that in nurseries heated by radiators and ventilated by natural means, the problem of controlling the humidity is difficult, particularly in cold weather. Not infrequently the relative humidity is lowered to 15 per cent or less as a direct result of artificial heating. A large quantity of water must be evaporated to raise the relative humidity to 65 per cent, and this can be accomplished satisfactorily only by the use of mechanical humidifiers, the reason being that the actual moisture content of cold outdoor air is very low compared with what is required indoors. For example, if a room 12 by 15 by 10 feet is to be kept at 77 F. and at a relative humidity of 65 per cent when the outdoor temperature is 20 F. and the outdoor relative

humidity 65 per cent, it would be necessary to evaporate a minimum of 3 pounds of water per hour in order to maintain the desired humidity. This is with natural ventilation through windows and doors to the extent of about two changes of air per hour. With twenty-five changes of air per hour, as in this investigation, 37½ pounds or 4½ gallons of water must be evaporated per hour to produce the optimum result. From these figures it is easy to see that evaporation from a pan of water on the radiator or from a wet sheet would be entirely inadequate.

In table 2 are given the minimum, maximum and average temperatures which, with a suitable range in humidity, permitted stabilization of body temperature in the various groups of infants. It can be seen that with a constant dew point of 64 F. (corresponding to an absolute humidity of 90 grains of moisture per pound of air) the environmental

TABLE 2.—*Air-Conditioning Requirements of Premature Infants, Infants' Hospital (Boston), 1926-1929*

Weight Groups, Pounds	Normal Premature Infants: Room Temperatures, F. (Dew Point, 64 F.; Air Movement, 15 Feet a Minute)			Congenitally Diseased Infants: Incubator Temperatures, F. (Relative Humidity of Room, 65%; Air Movement, 15 Feet a Minute)		
	Minimum	Maximum	Average	Minimum	Maximum	Average
1.5–1.9	83	88	86.0	86	100	93.5
2.0–2.4	82	87	84.5	86	98	90.5
2.5–2.9	78	86	83.0	84	95	88.0
3.0–3.4	77	86	80.5	79	90	83.5
3.5–3.9	75	85	78.5	79	88	81.0
4.0–4.4	75	85	77.0	78	86	79.0
4.5–4.9	75	85	76.0	76	85	77.0
5.0 and over	..	80	....	..	85	....

temperature requirements of the normal premature infants varied from 88 to 75 F., or over a range of 13 F. For the congenitally diseased groups, the corresponding range was 24 F.

Table 3 shows how a single central apparatus, furnishing conditioned air at 64 F. dew point to two nurseries, was made to meet the requirements of all the infants. Normal premature infants weighing from 1½ to 3½ pounds were cared for in the smaller nursery in an atmosphere of from 80 to 85 F. and a corresponding relative humidity of from 59 to 50 per cent. The larger group of normal premature infants—those weighing from 3½ to 5 pounds—occupied the larger nursery where the temperature was 77 F. and the relative humidity 65 per cent.

Since the congenitally diseased premature infants who were treated at any one time were comparatively few, they were cared for in electric incubators which were placed inside the larger nursery with tops open and the heat adjusted according to individual needs. In individual

patients the temperature in the incubator required before satisfactory levels of body temperature were established was sometimes as high as 100 F.

Summarizing the results of a four year study of the influence of air conditions on body temperature, it was found that the relative humidity best suited to the needs of premature infants is about 65 per cent. With this humidity, the temperature requirements ranged from 75 to 100 F., depending on the general condition of the infant and the body weight. A humidity of about 30 per cent or less tended to promote instability of body temperature and produced other untoward effects and fatalities, as will be shown later.

TABLE 3.—*Air-Conditioning Schedule Adopted for Nurseries for Premature Infants of Infants' Hospital (Boston)*

Classification of Infants	Weight Groups, Pounds	Temperature, F.	Relative Humidity, per Cent	Air Movement, Feet per Minute	Method of Treatment
Congenitally diseased and malformed infants	1.5-5.0	(86-100)*	†	15	Infants placed in open top incubators inside large nursery and heat gradually adjusted according to requirements
Normal premature infants	1.5-3.4	80-85	50-50	15	Infants placed in small room and room temperature adjusted according to requirements; hot water bottles (110 F.) used in special cases
	3.5-4.9	77	65	15	Infants placed in large nursery; hot water bottles (100 F.) used sparingly in special cases
	5.0 and over	70-74	Ward	Ward	With exception of definite cases of hypothermia, infants are removed to wards

* Incubator temperatures taken between basket and metal wall.
† Infants breathe cool room air at about 65 per cent relative humidity.

STABILIZATION OF BODY TEMPERATURE

Comparative data on stabilization of body temperature in the unconditioned and air-conditioned nurseries are given in figure 7 and tables 4 and 5. Figure 7 shows the fluctuations in body temperature of two premature infants, an infant (case 1) from the unconditioned nursery before the installation of the air-conditioning apparatus (1925) and an infant (case 2) from the conditioned nursery (1926). Both infants in whom clinical evidences of infection were not apparent were of practically the same fetal age and the same weight. The patient in case 1 was admitted on the seventh day after birth, and the body temperature fluctuated between 96 and 104 F. in spite of efforts to stabilize it in an electric bed with electric pads and hot water bottles in a well heated room. The patient in case 2 was admitted on the fourth day after birth. The environmental temperature for the first week was 80 F. and the relative humidity, 30 per cent. The body temperature rose gradually

from about 95 F. on admission to 99.5 F. without the application of extra heat, and after two days it became stabilized around 98.3 F. with a maximum variation of about 1.5 F., as compared with 7 F. for the patient in the unconditioned nursery.

Table 4 shows the fluctuations in body temperature of two comparable groups of infants. The patients in group 1 were selected from the 1925 records, prior to the installation of the air equipment, and those in group 2 from the 1926 records after the installation. Each group consisted of twelve infants weighing from 2 pounds, 10 ounces to 4 pounds, 6 ounces. In group 2 the air conditions were alternated each week between 77 F. with 65 per cent relative humidity, and 80 F. with 30 per cent relative humidity. In table 4 are shown the mean weekly minima, the mean weekly average and the mean weekly maxima

TABLE 4.—*Fluctuations of Body Temperature in Unconditioned and in Conditioned Nurseries Among Two Groups of Comparable Infants* *

Weeks After Admission to Nursery	Group 1 Unconditioned Nursery, 1925				Group 2 Conditioned Nursery, 1926			
	Mean Weekly Body Temperature, F.			Mean Maximum Fluctuation	Mean Weekly Body Temperature, F.			Mean Maximum Fluctuation
	Minimum	Average	Maximum		Minimum	Average	Maximum	
1st day	96.4	98.4	99.9	3.5	96.4	98.0	99.6	3.2
1	97.3	98.9	101.2	3.9	97.3	98.3	99.8	2.5
2	97.6	99.0	101.2	3.6	97.5	98.5	99.6	2.1
3	97.2	99.0	100.6	3.4	97.7	98.6	99.7	2.0
4	97.2	99.1	101.3	4.1	97.7	98.6	99.6	1.9
5	97.5	99.1	100.8	3.3	97.8	98.7	99.8	2.0
6	97.3	99.0	100.8	3.5	97.9	98.8	99.7	1.8
7	97.9	99.1	100.8	2.9	97.7	98.8	100.0	2.3
8	97.6	98.9	100.5	2.9	97.7	98.7	99.7	2.0

* Each group is composed of twelve infants.

of the body temperature, computed as follows: Individual readings of body temperature were averaged for the day (six readings a day) and then for the week. The mean of the weekly averages for the twelve infants is thus the mean weekly average for the group. The mean weekly minima were obtained by taking the lowest temperature recorded for each infant at any time during the week and averaging these twelve lowest values. The mean weekly maxima were computed in a similar manner. On admission, the patients in both groups showed approximately equal fluctuation in body temperature (table 4); but after the first week, the fluctuation in the body temperature of the patients in the conditioned nurseries settled down to about 2 F., as compared with 3.5 F. for the group in the unconditioned nursery. The average maximum body temperature in the unconditioned nursery always exceeded 100 F., whereas in the conditioned nurseries it was below 100 F.

Table 5 shows similar data on all infants (from the date of admission to the date of discharge) treated in the unconditioned and in the condi-

tioned nurseries from 1923 to 1930, except those dying from acute infections and congenital anomalies incompatible with life. It will be observed that as the infants grew in weight the number of cases steadily increased until the infants reached 5 pounds in weight. Thereafter, as they were discharged, the total number of cases decreased.

The data (fig. 7 and tables 4 and 5) reveal that stabilization of body temperature in the conditioned nurseries was obtained chiefly by preventing the infants from being overheated. The overheating of the patients in the unconditioned nursery presumably was due to inadequate control of the temperature and the large capacity for heat of the heating devices used (incubators, heated beds and hot water bottles), as well as to insufficient ventilation, a lack of facilities for cooling the room in

TABLE 5.—*Fluctuation of Body Temperature in Unconditioned and in Conditioned Nurseries*

Body Weight at Beginning of Each Week, Pounds	Unconditioned Nursery (1923-1925) Natural Humidity					Conditioned Nurseries (1926-1929) Relative Humidity (50-75%)				
	Number of Observations	Mean Weekly Body Temperature, F.			Mean Maximum Fluctuation	Number of Observations	Mean Weekly Body Temperature, F.			Mean Maximum Fluctuation
		Minimum	Average	Maximum			Minimum	Average	Maximum	
1.5-1.9	0	....	....	.....	...	1	96.7	98.0	99.7	3.0
2.0-2.4	2	96.0	98.7	102.3	6.3	9	96.1	98.0	99.7	3.6
2.5-2.9	11	97.1	98.8	101.4	4.3	23	96.4	98.2	99.9	3.5
3.0-3.4	26	97.4	99.1	101.6	4.2	48	96.9	98.3	99.8	2.9
3.5-3.9	44	97.3	98.8	100.9	3.6	84	97.2	98.4	99.7	2.5
4.0-4.4	49	97.3	99.0	100.8	3.5	103	97.5	98.5	99.6	2.1
4.5-4.9	55	97.6	99.1	100.9	3.3	103	97.6	98.7	99.9	2.3
5.0-5.4	51	97.6	98.7	100.3	2.7	63	97.7	98.7	99.9	2.2
5.5-5.9	39	97.5	98.7	100.4	2.9	31	97.7	98.6	99.9	2.2
6.0 and over	33	97.6	98.7	100.2	2.6	15	97.9	98.7	99.8	1.9

warm weather and the low humidities which prevailed. It may also have resulted from an attempt to raise the body temperature too quickly to the supposedly normal level of 98.6 F.—a practice which often leads to overheating (example, case 1, fig. 7).

The fluctuation in body temperature is, of course, not the same in all infants. It varies considerably according to weight and the length of residence in the nurseries (tables 4 and 5). The fluctuation of body temperature in small infants is quite high (table 5), decreasing progressively as the infants gain weight. When a weight of about 4 pounds is reached, the fluctuation in the conditioned nursery settles down to about 2 F., and this average is maintained, more or less, thereafter.

The range of variation in table 5 probably represents the average normal diurnal fluctuation in body temperature in premature infants. It is apparent that the fluctuations occur with some degree of regularity, and, as will be shown further on (table 10, column 7), such fluctuation in body temperature is accompanied by a satisfactory gain

in weight. In spite of fluctuations of from 3 to 3.5 F., infants weighing between 2 and 3 pounds gained on an average 3⅕ ounces a week, on a food intake of about 50 calories per twenty-four hours per pound of body weight. Hess [17] regarded daily fluctuations greater than 1.5 F. as dangerous. Reiche,[18] on the other hand, stated that daily fluctuations of from 11.3 to 18 F. (from 6.3 to 10 C.) have been observed in the first days of life of premature infants, in consequence of initial loss of heat, and that these fluctuations may persist in a lesser degree for weeks. Even in normal infants, Schelble [9] found that the diurnal fluctuation is about 1.5 F., when the temperature is recorded twice daily, and he stated that the fluctuation would have been greater had he recorded the temperature more frequently.

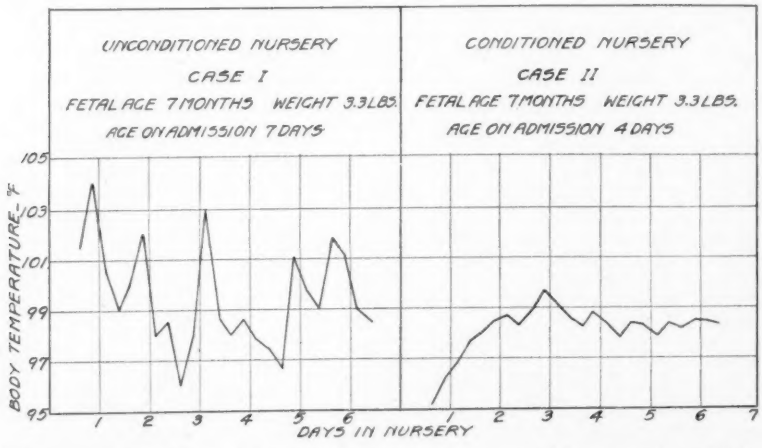

Fig. 7.—Fluctuation of body temperature in unconditioned and conditioned nurseries.

There is much discussion in the literature as to whether the tendency toward a subnormal body temperature in premature infants is a constitutional peculiarity or whether it is the result of exposure to unfavorable environmental conditions. According to the present study, the former argument seems to hold true more generally. Even under what are believed to be the most favorable atmospheric conditions, the body temperature (rectal) became stabilized, as a general rule, at a level lower than 98.6 F. Moreover, a definite relationship existed between the mean weekly body temperature and the mean weekly body weight,

17. Hess, J. H.: Premature and Congenitally Diseased Infants, Philadelphia, Lea & Febiger, 1922.

18. Reiche, A.: Der initiale Wärmeverlust (Erstarrung) bei frühzeitig geborenen und "lebensschwachen" Kindern, Deutsche med. Wchnschr. **44**:491, 1918.

as shown in table 5, columns 1 and 9. According to these data, there is apparently a favorable but varying body temperature, the variation following closely the body weight. From a comparatively low level of about 98 F. (rectal), the average body temperature of infants weighing about 2 pounds rose progressively as the weight increased, but the temperature of 98.6 F. was not attained until the infants reached a weight of about 5 pounds. This weight is generally taken as the boundary line separating the premature from the full-term infant.

It should be emphasized that in the low weight group of infants those with the persisting low body temperature showed an adequate temperature regulation and a satisfactory growth. These observations suggest that a body temperature of the order shown in table 5 is probably a characteristic of prematurity which should not be interfered with. In other words, the object should be to stabilize the body temperature regardless of the level at which stabilization takes place. This peculiar diathesis of premature infants was emphasized by Eckstein [11] after he observed a range below the accepted normal level.

In summarizing the results, data over a seven year period show that the body temperature of premature infants can be controlled much better and much more easily in nurseries in which the air temperature, humidity and ventilation rate are automatically controlled. The fluctuation in body temperature of infants in the conditioned nurseries was less than that in the unconditioned nursery, particularly in the case of the smaller infants.

A definite relationship was found to exist between the body temperature and the fluctuation in body temperature and weight. For low weight groups, the body temperature, as a general rule, was 98 F., and the fluctuation was comparatively high. As the weight increased, the body temperature rose and the fluctuation decreased progressively. When a weight of 5 pounds was reached, the temperature curve flattened close to 98.6 F., and the fluctuation settled down to about 2 F. From then on the reaction of premature infants to environment was similar to that of full-term infants.

The predisposition to a subnormal temperature, particularly in infants of the low weight group, is believed to be a characteristic of prematurity which should be preserved. Attempts to force the body temperature of small infants to the supposedly normal level of 98.6 F. should be discouraged, as in a number of instances such a practice has been followed by overheating with its resultant serious consequences. We believe under such circumstances that excessive environmental temperature is the causative factor, as we have observed this effect in both high and low humidity.

GROWTH UNDER VARIOUS CONDITIONS [19]

In this section data are presented with reference to the growth of premature infants under three different sets of air conditions, namely, those in the old nursery prior to the installation of the air-conditioning apparatus (1923 to 1925) and those in the conditioned nurseries (1926 to 1929) under accurately controlled air conditions of high and low humidity.

Since the indexes of growth are affected considerably by the type and amount of food, it is important that the dietary schedule be given in detail. Nutrition, especially in the earlier days of life before the circulatory and respiratory organs have had an opportunity to accommodate themselves to the extra-uterine environment, is not, in our opinion, a very important factor in the preservation of life in premature infants. Therefore, during this period of adaptation on the first day of life, food was not given, as a rule, but the loss of body fluid was offset by the administration of water or of a 5 per cent solution of dextrose. On the second and third days, the infants were fed either woman's milk or the standard mixture of cow's milk, while at the same time full fluid requirements were maintained (p. 1178).

As the infants adjusted themselves to the atmospheric environment, the caloric value of the food was increased gradually to the total amount necessary to produce a satisfactory gain in weight. With the exception of the first few months in 1926, as stated previously, the average amount has not exceeded 60 calories per pound of body weight for twenty-four hours.

This comparatively low caloric value has proved sufficient to meet the requirements for growth under controlled atmospheric conditions. Considerably higher caloric values have been used in the old unconditioned nursery, as will be shown later. The representative feeding schedules are given in table 6. It should be made clear that these schedules represent the standards which were established for the purpose of this study and that they do not necessarily imply the quantities

19. It should be clearly understood that we have appreciated the difference between the premature infants studied by us and infants born in maternity hospitals or homes who can be immediately transferred to quarters already prepared without exposure to "chilling" and infection. Therefore, on account of the inaccuracy of the information as to the fetal age and the weight and length at birth, our statistics concerning the relation of various air conditions to the growth and developmental patterns of premature infants should not be taken as representative of infants who have had institutional care from the start. It is hoped that more representative information along these lines will be published shortly by Dr. Stewart H. Clifford from the Boston Lying-Inn Hospital, where an air-conditioning system has been in use since 1931. There, infants born prematurely are conveyed to controlled environmental surroundings directly after delivery and such variable factors as we have had to contend with have been largely eliminated.

of food which premature infants are capable of utilizing. It is perhaps necessary to mention that although an endeavor was made to follow a standardized feeding schedule for the purpose of securing comparable results situations arose which made it necessary from time to time to vary the amount of each feeding, the caloric value and the interval of feeding. This was particularly true in the first ten days of life, and during the periods when special foods were used for therapeutic purposes.

Physiologic Loss of Weight.—There were forty-eight infants admitted on the first day of life whose weight at birth had been recorded. In thirty-six of these patients (75 per cent), the lowest weight was reached on the fourth day of life and in the remaining twelve (25 per cent) the loss in weight continued for from five to eight

TABLE 6.—*Representative Feeding Schedule for Infants Given Mixture or Woman's Milk* *

New-Born Infants		Infants Over 1 Week Old on Admission	
Day of Life	Calories per Pound per 24 Hours	Day of Admission	Calories per Pound per 24 Hours
1st	0	1st	0-30
2d	10	2d	20-30
3d	20	3d	30
4th	30	4th	35
5th	40	5th	40
6th to 10th	50	6th	45
After 10th	55 to 60	7th	50
		After 7th	50-60

* The usual routine after the first twelve to twenty-four hours was to administer 1 drachm of fluid every two hours, increasing by 1 drachm until a total of from ½ to 1 ounce was being given at each feeding. The feeding interval was then lengthened to three or four hours, and woman's milk or a standard formula was gradually substituted for the fluid (sterile water or 5 per cent dextrose).

days after birth. In the latter group of patients the additional loss, after the fourth day, was about 1 ounce. It never exceeded 2 ounces. The period of time over which the initial loss continued was an average of four and six-tenths days in the unconditioned nursery and four and two-tenths days in the conditioned nursery under low humidity and three days under high humidity. The average under all air conditions was three and seven-tenths days. This is substantially in accord with the findings of Pfaundler [20] and Ramsey and Alley.[21] In a relative humidity between 50 and 75 per cent, two of the forty-eight infants gained in weight from the first day and three maintained their birth weights without the expected initial loss.

20. Pfaundler, M.: Körpermass-Studien an Kindern, Ztschr. f. Kinderh. **14**:1, 1916; quoted by Hess.[17]

21. Ramsey, W. R., and Alley, A. G.: Observations on the Nutrition and Growth of New-Born Infants: An Analysis of 300 Clinical Charts, Am. J. Dis. Child. **15**:408 (June) 1918.

Humidity in Relation to Initial Loss of Weight.—The average loss in weight under various conditions of humidity, given in table 7, was computed by subtracting from the weight at birth the minimum weight reached at any period during the first four days. The patients in the unconditioned nursery suffered the maximum loss, while the minimum loss of weight occurred in patients living in the conditioned nurseries under a relatively high humidity. These figures, shown at the bottom

TABLE 7.—*"Initial Loss" in Body Weight Under Various Air Conditions*

	Unconditioned Nursery (1923-1925) Natural Humidity			Conditioned Nurseries (1926 1929) Low Relative Humidity (25-49%)			Conditioned Nurseries (1926 1929) High Relative Humidity (50-75%)		
Approximate Birth Weight, Pounds	Number of Cases	Average Calories per Lb. in 24 Hrs. for Loss Period	Loss in per Cent of Birth Weight	Number of Cases	Average Calories per Lb. in 24 Hrs. for Loss Period	Loss in per Cent of Birth Weight	Number of Cases	Average Calories per Lb. in 24 Hrs. for Loss Period	Loss in per Cent of Birth Weight
Under 3	0	..	....	11	14	10.2	3	19	9.3
3 to 4	5	21	12.7	4	11	8.8	10	12	6.1
Over 4	2	22	11.5	4	14	5.4	9	9	4.7
All weights	7	21	12.4	19	13	8.9	22	12	6.0

TABLE 8.—*Days to Regain Birth Weight Under Various Air Conditions*

	Unconditioned Nursery (1923-1925) Natural Humidity		Conditioned Nurseries (1926-1929) Low Relative Humidity (25-49%)		Conditioned Nurseries (1926-1929) High Relative Humidity (50-75%)	
Approximate Birth Weight, Pounds	Number of Cases	Days to Regain Birth Weight	Number of Cases	Days to Regain Birth Weight	Number of Cases	Days to Regain Birth Weight
Under 3.....	0	....	7	20.7	2	28.5
3 to 4.....	2	19.5	3	18.3	10	14.1
Over 4.....	2	33.5	4	18.3	8	13.0
All weights.....	4	26.5	14	19.5	20	15.1

of the table, are 12.4 and 6 per cent, respectively. Under low humidity the loss in weight of the patients was intermediate between these values.

The period of time required by the infants to regain their weight at birth varied in a similar manner (table 8). The average was twenty-six and five-tenths days in the unconditioned nursery; nineteen and five-tenths days in the conditioned nursery under low humidity, and fifteen and one-tenth days under high humidity.

Tables 7 and 8 show that the period and amount of initial loss in weight as well as the time required to regain the weight at birth vary in an inverse proportion to the weight at birth. In other words, expressed in percentage of the weight at birth, the less the weight, the greater is the relative loss and the longer the period taken for regaining

the original weight. This is in accord with Hammet's rule which has been confirmed by Cook [22] and others.

Gain in Weight Under Various Air Conditions.—Tables 9 and 10 show respectively the average amount of food expressed in calories per pound and the average gain in weight per week of patients living in (*a*) the unconditioned nursery, (*b*) the conditioned nurseries under low humidity, (*c*) the same nurseries under high humidity and (*d*) the general wards after graduation. The data include all infants treated in the nurseries between 1923 and 1929 except those dying from non-preventable diseases and those dying within the first forty-eight hours after admission. The gains in weight have not been corrected for the initial loss of weight or for any other loss resulting from vomiting, diarrhea and febrile periods.

TABLE 9.—*Weekly Average of Calories Administered in Twenty-Four Hours per Pound of Body Weight*

Weight at Beginning of Each Week, Pounds	Unconditioned Nursery (1923-1925) Natural Humidity	Conditioned Nurseries (1926-1929)		After Discharge to General Wards (1926-1929) Natural Humidity
		Low Relative Humidity (25-49%)	High Relative Humidity (50-75%)	
1.5-1.9	....	48.1	46.8	....
2.0-2.4	29.0	44.2	47.3	....
2.5-2.9	59.3	52.3	50.1	....
3.0-3.4	55.2	52.5	53.3	....
3.5-3.9	58.5	53.8	53.5	....
4.0-4.4	62.4	58.4	54.9	....
4.5-4.9	62.0	59.1	56.1	56.1
5.0-5.4	62.3	55.4	53.9	57.5
5.5-5.9	61.8	56.7	54.3	58.9
6.0 and over	63.0	52.9	54.9	57.6

It can be seen that the maximum gain in weight in the groups of patients weighing less than 5 pounds occurred in the conditioned nursery under high humidity. The gain in weight was less under low humidity and in the unconditioned nursery. The least gain occurred in the general wards after the patients had graduated from the conditioned nurseries. It should be pointed out that the caloric value of the food administered to the infants in the conditioned nurseries was 6 calories less per pound of body weight per twenty-four hours than that of the food received by the patients in the unconditioned nursery. Moreover, the average gains in weight of the premature infants in the conditioned nurseries (table 10) compare favorably with the average gains reported by other observers in instances in which a higher caloric intake of food prevailed.

Although it is not our purpose in this paper to discuss the general principles in the field of metabolism, it is of interest to point out that these observations support the belief that both the requirements of food

22. Cook, P.: A Clinical Study of the Premature Infant, Arch. Pediat. **38**:201, 1921.

and growth depend to a significant extent on the temperature and humidity to which the organism is exposed. As shown by McConnell, Yaglou and Fulton [23] and others, under fluctuating air conditions, below and above the optima, more energy is required to maintain body temperature, and body weight is likely to be affected, unless more food is administered and assimilated, since the extra energy has to be drawn directly from the body fuel depots.

In both old and new nurseries the gain in weight was somewhat greater among girls than among boys, as shown in table 11.

TABLE 10.—*Average Weekly Gains in Weight Under Various Air Conditions*

Weight at Beginning of Each Week, Pounds	Unconditioned Nursery (1923-1925) Natural Humidity		Conditioned Nurseries (1926-1929) Low Relative Humidity (25-49%)		Conditioned Nurseries (1926-1929) High Relative Humidity (50-75%)		After Discharge to General Wards (1926-1929) Natural Humidity	
	Number of Cases	Weekly Gain, Oz.	Number of Cases	Weekly Gain, Oz.	Number of Cases	Weekly Gain, Oz.	Number of Cases	Weekly Gain, Oz.
1.5-1.9	0	...	3	2.7	1	0.2	..	...
2.0-2.4	1	—7.0	5	1.0	9	2.8	..	...
2.5-2.9	11	1.6	13	1.1	23	3.4	..	...
3.0-3.4	26	3.2	13	2.8	48	3.3	..	...
3.5-3.9	44	2.9	14	3.9	84	4.1	..	...
4.0-4.4	49	4.3	26	3.0	103	4.5	..	...
4.5-4.9	55	4.3	27	3.4	103	5.4	14	2.7
5.0-5.4	51	5.6	18	5.9	63	5.0	35	4.4
5.5-5.9	39	5.8	10	6.9	31	5.0	20	3.4
6.0 and over	33	3.6	8	6.6	15	4.7	31	4.8

TABLE 11.—*Average Weekly Gain in Weight According to Sex*

Weight Groups, Pounds	Unconditioned Nursery (1923-1925) Boys		Unconditioned Nursery (1923-1925) Girls		Conditioned Nurseries (1926-1929) Boys		Conditioned Nurseries (1926-1929) Girls	
	Number of Cases	Weekly Gain, Oz.	Number of Cases	Weekly Gain, Oz.	Number of Cases	Weekly Gain, Oz.	Number of Cases	Weekly Gain, Oz.
Under 2.5	0	...	1	—7.0	4	1.5	6	2.6
2.5-3.9	28	2.4	24	3.2	45	3.6	53	3.8
4.0-5.4	34	4.8	26	4.5	63	5.2	63	4.9
5.5 and over	35	4.5	24	5.0	43	4.9	34	6.1

Optimum Air Conditions in Relation to Gain in Body Weight.—In table 10, it can be seen that the gain in weight is comparatively small among the patients in the lowest weight groups and that it increases progressively as the infants grow larger. Although for patients in the groups weighing less than 5 pounds the gain in weight is greater under high than under low humidity, the reverse holds true for patients in the groups weighing more than 5 pounds. This aspect of the situation is further supported by the data in figure 8 which shows composite growth

23. McConnell, W. J.; Yaglou, C. P., and Fulton, W. B.: Basal Metabolism Before and After Exposure to High Temperatures and Various Humidities, Pub. Health Rep. **39**:3075 (Dec. 5) 1924.

curves for the observations made on high and low humidity under strictly comparable conditions.

In figure 8, the comparison is restricted to infants who were exposed to both high and low humidities during the period in which high and low humidity was being alternated weekly, biweekly or triweekly. In constructing the weight curves, the infants were classified in four groups according to the weight on admission. To the average initial weight of each group were added the average weekly gains in weight of the group, week after week, until the majority of infants were discharged.

A most interesting fact to be observed is the decreasing importance of high humidity with increase in body weight. Whereas it can be seen

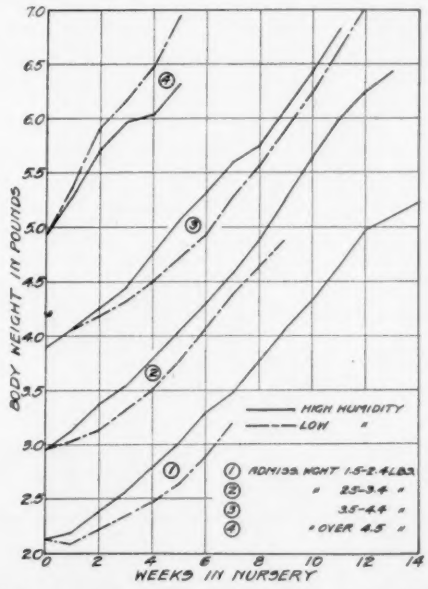

Fig. 8.—Comparative growth of premature infants under high and low humidity.

that infants who weighed less than 4½ pounds on admission gained more rapidly under high than under low humidity, the reverse was true of the infants whose weight on admission was 4½ pounds or over. The latter group consisted largely of congenitally diseased infants whose weight at birth and at admission approached 5 pounds, but the fetal age and the age at admission varied over a wide range.

This reversal of the effect of humidity was not confined to congenitally diseased premature infants but occurred in all premature infants as they approached or exceeded 5 pounds in weight. Further evidence in support of this particular point is presented in table 12, which gives the average weekly gain in weight under low and high humidity in two groups of infants weighing 5 pounds or more. Comparison is again

restricted to infants who have been exposed to alternating conditions of humidity. The total number of cases in group 2, table 12, is less than that in figure 8, because many infants were discharged before attaining a weight of 5 pounds. Group 2 includes all infants with weights between 1½ and 4½ pounds on admission who were not discharged until after they reached the critical weight of 5 pounds. It can be seen that in both groups the gain under low humidity is greater than that under high humidity. In group 2, while the difference is not great, it is consistent. The relative coolness of the low humidity may account for the greater gain in weight among the premature infants weighing 5 pounds, just as adults find a combination of 80 F. temperature with 30 per cent relative humidity, although somewhat too warm for comfort, considerably cooler than one of 77 F. temperature with 65 per cent relative humidity.[15] Therefore, we are not at all justified in concluding that a relative humidity of 30 per cent is the best for these premature

TABLE 12.—*Average Weekly Gains in Weight of Premature Infants, Weighing 5 Pounds or More, Under Low and High Humidity*

	Number of Cases	Low Relative Humidity (80 F., 30%) Oz. per Week	High Relative Humidity (77 F., 65%) Oz. per Week
Group 1: Infants weighing approximately 5 pounds on admission	9	7.8	5.4
Group 2: Infants weighing between 1.5 and 4.5 pounds on admission	17	5.8	5.1

infants until we have had an opportunity to try out a relative humidity of 65 per cent, in combination with a temperature lower than 77 F., for instance 70 or 72 F. Owing to limitations in equipment, this as yet has not been possible.

It might be inferred from these data that it is well to maintain during the first stage of the extra-uterine development of the premature infant a moist environment simulating the intra-uterine environment to which the infant would have been exposed. When a premature infant reaches a weight of 5 pounds, his physiologic functions are adequately stabilized, subcutaneous fat has increased, the sweat glands respond normally, and he therefore requires an environment more or less comparable to that of the full-term infant.

Growth in Length in Relation to Physical Characteristics.—As mentioned previously, the length of premature infants, with few exceptions, was measured regularly at the time of admission and at weekly intervals throughout the infant's residence in the conditioned nurseries. The technic of measurement used was subject to a possible maximum error of 0.5 inch.

In tables 13 to 16 are presented the average monthly increases in length according to estimated fetal age, age on admission, length and weight at the time of admission. According to these data, it appears that the maximum rate of growth in length takes place during the first and second month, and during the next month the rate is but slightly increased. The average increase in length varies from 0.65 inch for

TABLE 13.—*Monthly Increase in Length of Premature Infants According to Fetal Age (1926-1929)*

Fetal Age, Months	First Month		Second Month		Third Month	
	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches
Under 7	12	0.66	10	1.09	7	1.22
7 to 8	47	0.65	30	0.96	15	1.13
8 and over	33	0.64	18	1.00	4	1.02
Unknown	4	0.63	4	0.88	..	....
All fetal ages	96	0.65	62	0.99	26	1.14

TABLE 14.—*Monthly Increase in Length of Premature Infants According to Age on Admission (1926-1929)*

Age on Admission	First Month		Second Month		Third Month	
	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches
2 days or less	27	0.61	20	0.98	9	1.17
3 to 15 days	44	0.71	29	1.01	10	1.15
16 to 30 days	16	0.63	9	1.00	4	1.32
31 days and over	9	0.49	4	0.91	3	0.78
All ages	96	0.65	62	0.99	26	1.14

TABLE 15.—*Monthly Increase in Length of Premature Infants According to Length on Admission (1926-1929)*

Length on Admission, Inches	First Month		Second Month		Third Month		Fourth Month	
	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches
Under 15	9	0.50	9	1.00	9	1.26	3	1.82
15.0 to 16.4	34	0.66	29	1.09	13	1.13	0	....
16.5 to 17.9	44	0.65	23	0.86	4	0.91	0	....
Over 18	9	0.69	1	1.00	0	....	0	....
All lengths	96	0.65	62	0.99	26	1.14	3	1.82

the first month after admission to 1.14 inches for the third month. Friedenthal [24] reported much higher values, ranging from 2.37 inches (6 cm.) per month for fetal ages of from 6 to 7 months to 1.57 inches (4 cm.) for full-term infants.

The rate of growth in length shows a better correlation with body weight than with any other of the physical factors studied. In table 16 it may be seen that when the infants are classified according to the

24. Friedenthal, H.: Med. Wchnschr., 1909, no. 34; quoted by Hess,[17] p. 45.

weight on admission, the growth in length for the first month increases progressively with the weight. The increase in length during the second month is about the same in all weight groups; in the third month it decreases with increasing body weight.

When the infants are classified according to the age on admission, as in table 14, the growth in length is irregular. The relationship between the length and rate of growth in length (table 15) and that

TABLE 16.—*Monthly Increase in Length of Premature Infants According to Weight on Admission (1926-1929)*

Weight on Admission, Pounds	First Month		Second Month		Third Month	
	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches
1.5 to 2.4	7	0.46	7	1.09	7	1.22
2.5 to 3.4	40	0.56	36	0.92	16	1.14
3.5 to 4.4	42	0.75	18	1.06	3	0.93
4.5 and over	7	0.78	1	1.10	0	....
All weights	96	0.65	62	0.99	26	1.14

TABLE 17.—*Monthly Increase in Length of Premature Infants According to Sex (1926-1929)*

Sex	First Month		Second Month		Third Month	
	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches	No. of Cases	Increase, Inches
Boys	45	0.67	28	1.07	14	1.11
Girls	51	0.63	33	0.93	12	1.17

TABLE 18.—*Monthly Increase in Length Under High and Low Humidity Conditions in a Group of Twenty-Seven Infants*

	First Month, Inches	Second Month, Inches	Third Month, Inches
High relative humidity (50-75%)	0.69	1.05	1.13
Low relative humidity (25-49%)	0.50	1.05	1.38
Average body weight	3.8 pounds	5.0 pounds	6.2 pounds

between fetal age and rate of growth in length (table 13) are of but little practical value.

Table 17 shows no striking difference between the growth in length of male and of female premature infants. For the first and second month after admission, the increase in length among boys is slightly greater than that among girls, and during the third month it is slightly less.

Humidity in Relation to Growth in Length.—Table 18 shows that the effect of humidity on growth in length is similar to its effect on growth in weight. The data were secured from observations on twenty-seven patients on whom weekly measurements of length were made

throughout residence in the conditioned nurseries, during the period in which the conditions were changed alternately from high to low humidity.

In computing the average monthly gains in length under the alternating conditions of humidity, the individual weekly gains were first tabulated separately for high and low humidity according to the time of residence in the hospital in weeks. The gains for each week were then averaged separately for high and low humidity. The monthly gains were finally computed by adding the average weekly gains for four weeks and two-sevenths of the average gain for the fifth week. The corresponding average body weight was computed as in figure 8.

It can be seen (table 18) that the increase in length for the first month is considerably higher under high than under low humidity. In the second month the increase is the same for both humidities. In the third month the effect of humidity is reversed, the increase in length being greater under low than under high humidity. A glance at the corresponding average body weights discloses the close association of this effect of humidity with the critical weight of 5 pounds, as was the case with growth in weight. A high humidity is therefore more favorable for an increase in length among infants weighing less than 5 pounds. This indication is in accord with Romanoff's study [25] on the influence of humidity on the development of the chick embryo. He found that "the calcium metabolism at the early stages of embryonic development was much better at high than at low humidity."

Weight-Length Relationship in the Growth of Premature Infants.—In table 19 is given the average relationship between weight and length as well as the maximum range in length for any given weight group. There seems to be no difference between the average lengths of boys and girls who have the same body weight, nor in the weight-length ratio of the two sexes. Therefore, a more representative average relationship may be obtained by combining the data for both sexes.

The weight-length ratio is considered to be an index of the general solidity or robustness of the body, and it is sometimes used as an index of the nutritional status and expectancy for life of the infant. This ratio may be computed by dividing the weight in pounds by the length in inches, and the result represents the weight per unit length.

The range in length in columns 5 and 9 (table 19) is so great, especially in girls, that it is difficult to conjecture as to the variation from the average which may be considered either normal or abnormal.

25. Romanoff, A. H.: Biochemistry and Biophysics of the Developing Hen's Egg: I. Influence of Humidity, Cornell Univ., Agric. Exper. Stat., Mem. 132, May 16, 1930.

It is a well known fact that an increase in length is not necessarily coincident with an increase in weight. It may even take place with an actual loss in weight. At times, an apparently normal infant may show a satisfactory gain in weight but no increase in length for as long as seven consecutive weeks without showing any demonstrable harmful effects during or after the period of retarded growth in length. According to Talbot and his co-workers,[6] the length of the body is an unreliable index for predicting the basal metabolism of premature infants. According to our data, it also appears to be an unsatisfactory index of growth and of vitality. Theoretically, the weight-length ratio should provide a better index than either length or weight alone, but actually, owing to the wide individual variations in length and the difficulty of measuring body length accurately, its value during the early stage of development is questionable. Weight, on the other hand, is an accu-

TABLE 19.—*Average Relation of Weight to Length (1926-1929)*

Weight Groups, Pounds	Boys				Girls			
	No. of Cases	Length, Inches	Weight-Length Ratio	Maximum Range, Inches	No. of Cases	Length, Inches	Weight-Length Ratio	Maximum Range, Inches
1.5-1.9	1	13.6	0.125	.....	7	13.4	0.127	12.6-14.0
2.0-2.4	9	14.9	0.148	14.4-15.5	12	14.5	0.152	13.5-15.5
2.5-2.9	16	15.6	0.173	14.8-17.0	26	15.8	0.171	14.4-19.3
3.0-3.4	26	16.2	0.197	15.3-17.3	32	16.3	0.196	15.1-19.0
3.5-3.9	44	17.0	0.218	15.0-18.9	49	17.0	0.218	15.0-18.5
4.0-4.4	51	17.4	0.242	16.3-18.5	51	17.3	0.243	16.0-19.0
4.5-4.9	44	17.9	0.262	16.9-19.3	48	18.0	0.261	16.7-19.3
5.0-5.4	26	18.4	0.283	17.3-19.6	22	18.4	0.283	17.0-20.0
5.5-5.9	10	18.9	0.302	18.0-20.2	6	19.0	0.300	18.5-20.0

rately and easily determined quantity, and it is admittedly a most suitable index in judging the progress of the premature infant. A regular gain in weight should be considered as evidence of growth and health.

Duration of Residence in the Unconditioned and Conditioned Nurseries.—Perhaps the most interesting figures in table 20 are those in connection with patients having a weight on admission of less than 2½ pounds. It can be seen that from 1923 to 1926 no patients of this weight group survived to be discharged from the unconditioned nursery, whereas from 1926 to 1929 three patients weighing between 1½ and 2 pounds and five patients weighing between 2 and 2½ pounds were discharged from the conditioned nurseries. The average residence of these two groups was one hundred and twenty-three and seven-tenths and eighty-seven and two-tenths days respectively.

The length of residence depended largely on the weight at the time of admission (table 20). It decreased progressively with increasing weights on admission, and on an average the residence in the conditioned nurseries was about 18 per cent less than that in the unconditioned nursery.

INFLUENCE OF AIR CONDITIONS ON DIGESTIVE DISORDERS

While it is not within the scope of this communication to describe diseases to which premature infants are peculiarly susceptible, it is necessary that some consideration be given to the disturbing frequency with which symptoms directly referable to the gastro-intestinal tract occur. While environment—that is, temperature, humidity and movement of air—has been recognized as a factor predisposing to derangements of this regional system,[26] direct scientific proof of the relationship in premature infants has not been obtainable, previously, under circumstances in which the air conditions have been controlled automatically.

A critical review of the records of patients in the unconditioned nursery together with observation of the patients living in the conditioned nurseries under low humidity shows clearly that air conditions in general and low humidity in particular exert a conspicuous influence in initiating symptoms referable to the digestive tract. Furthermore, it has been possible, on the basis of these studies, to outline the sequence of events which so often lead to a fatal outcome.

TABLE 20.—*Average Residence in Unconditioned and in Conditioned Nurseries*

Weight on Admission, Pounds	Unconditioned Nursery (1923-1925)		Conditioned Nurseries (1926-1929)		Reduction, per Cent
	Number of Cases	Days in Nursery	Number of Cases	Days in Nursery	
1.5-1.9	0	....	3	123.7	....
2.0-2.4	0	....	5	87.2	....
2.5-2.9	3	73.7	21	76.3	(+3.5)
3.0-3.4	16	66.1	22	56.9	13.9
3.5-3.9	13	63.5	30	53.3	16.1
4.0-4.4	10	50.9	28	40.9	19.6
4.5 and over	17	50.2	23	27.4	45.4

The early signs indicative of a disorder of the gastro-intestinal tract, or as we prefer to designate it, a "digestive syndrome," are apathy or general bodily inactivity, refusal of food and regurgitation or vomiting of food together with an increase in the number and alteration in the character of stools. A continuation of any one or any combination

26. Among other observers, Helmholz (The Relation of Heat to the Morbidity and Mortality of Infants from Gastro-Intestinal Diseases, J. A. M. A. **63**:1371 [Oct. 17] 1914), McClure and Sauer (Clothing as a Factor in the Production of Heat Stasis, Am. J. Dis. Child. **9**:490 [June] 1915), Wilkinson and Todd (External Heat Cause of Fever in Children, J. A. M. A. **88**:787 [March 12] 1927) and one of us (C. P. Y.) (Atmospheric Conditions: General Considerations, Report of the Committee on Growth and Development of the White House Conference on Child Health and Protection, New York, Century Company, 1931, pt. 1, p. 255) have called particular attention to environmental factors as a predisposing cause for the high morbidity of gastro-intestinal and respiratory diseases among infants during the first two years of life.

of these clinical manifestations is invariably succeeded by instability of the body temperature and failure to maintain the average gain in weight.

Experience has taught us that if these clinical signs of disturbed physiologic function are not corrected they are followed frequently by persistent vomiting, profuse diarrhea, rapid loss of weight, fever and, finally, the development of the classic picture of dehydration and acidosis. In the early stage, as a rule, focal or systemic infections cannot be detected; polymorphonuclear leukocytosis is not present, blood cultures are sterile, and pathogenic organisms cannot be recovered from the urine and feces by culture. But at any time secondary infection may set in. In nearly all infants who succumbed, there was found at necropsy pathologic evidences of extensive and overwhelming infection —especially of the respiratory system.

During the periods from January to June, 1926, and from January to June, 1927, when the relative humidity in the conditioned nurseries was being alternated weekly or biweekly from 30 to 65 per cent, it was observed that a few premature infants reacted adversely to the low humidity of 30 per cent. There were noticeable increase in frequency of vomiting and in the number of stools, instability of the body temperature and limitation of the average gain in weight or, in other words, the appearance of symptoms characteristic of the early stage of the digestive syndrome.

In order to throw more light on the relationship of these clinical signs to thermal environment, as the responsible factor, groups of selected patients who were not handicapped seriously by congenital deformities were observed in an environment of approximately 30 per cent humidity. The reactions of sixteen infants were studied over a period of from ten to twenty-five days. The body temperature was taken every four hours, and the weight was determined three times each week. The number, volume and character of the stools were recorded, and the frequency of vomiting was noted. The activity and general behavior of the infants were followed closely. The patients showed no evidences of focal or systemic infection so far as could be determined by clinical or laboratory means. The results of these observations were similar to those in the preceding period and corresponded in every respect with the sequence of events which occurred with such regularity in the unconditioned nursery. Of the sixteen babies, four were severely affected and five mildly affected. The remaining seven patients were apparently unaffected. It was found that the degree of reaction to the low humidity was related to the general physical state, the actual body weight and the length of time spent in the air-conditioned nursery.

In an environment with a relative humidity of between 50 and 65 per cent, symptoms referable to the gastro-intestinal tract were less frequent,

the disturbance was of shorter duration, and the attack subsided more rapidly. In comparison with the group of patients kept in low humidities and with the patients in the unconditioned nursery, the reaction was attended by far less serious consequences.

The conclusions as to the interrelation of various air conditions and gastro-intestinal symptoms are based on data secured from a relatively large number of premature infants who manifested unequivocal reactions to the periods of changing thermal conditions, according to an arbitrary standard designed especially for this purpose. The two essential signs of the digestive syndrome were (*a*) an increase in the total number of stools above an arbitrary number of twenty-eight stools per week, together with a change from formed or semiformed to loose

TABLE 21.—*Weekly Relative Incidence of "Digestive Syndromes" According to Body Weight and Relative Humidity*

	Unconditioned Nursery (1923-1925) Natural Humidity		Conditioned Nurseries (1926-1929)			
			Low Relative Humidity (25-49%)		High Relative Humidity (50-75%)	
Weight, Pounds	Total No. in Group	Per Cent of Incidence	Total No. in Group	Per Cent of Incidence	Total No. in Group	Per Cent of Incidence
1.5-1.9	0	....	3	33.3	1	....
2.0-2.4	1	....	5	20.0	9	11.1
2.5-2.9	11	36.4	13	53.8	23	4.3
3.0-3.4	26	23.1	13	23.1	48	12.5
3.5-3.9	44	22.7	14	14.3	84	9.5
4.0-4.4	49	20.4	26	23.1	103	10.7
4.5-4.9	55	23.6	27	14.8	103	8.7
5.0-5.4	51	11.8	18	5.6	63	15.9
5.5-5.9	39	17.9	10	30.0	31	12.9
6.0 and over	33	12.1	8	22.2	15	20.0
Average 2.5-3.9	..	27.4	..	30.4	..	8.8
4.0-4.9	..	22.0	..	19.0	..	9.7
4.0 and over	..	13.9	..	19.3	..	16.3
Average of all weights	..	21.1	..	22.9	..	11.6

watery stools, and (*b*) lessening of the average weekly gain, failure to gain or a loss in weight. We believe that the weight index is a necessary additional standard, as this measurement is invariably a most dependable index of disturbed physiologic function. As in the other studies, such variable factors as food, nursing care and clothing remained as uniform as possible, and patients with infection were excluded in the analysis of the results.

In table 21 is given the general weekly incidence of the digestive syndrome in (*a*) the unconditioned nursery, (*b*) the conditioned nursery with a low humidity and (*c*) the same nursery with a high humidity. The figures are tabulated according to the body weight at the beginning of each week. The incidence in columns 3, 5 and 7 was computed by dividing the number of cases of the digestive syndrome occurring in any given weight group by the corresponding total number of infants placed under the given environmental conditions.

By referring to table 21, it can be seen that the incidence of the digestive syndrome, as estimated according to the arbitrary standard, was at a minimum when the humidity was high and at a maximum when the humidity was low. The highest incidence was in the groups of premature infants weighing from 2½ to 3 pounds, in the unconditioned nursery and in the conditioned nursery under a relatively low humidity. Reversely, under high humidity, the lowest incidence occurred in premature infants weighing less than 5 pounds. It is interesting to note that in this environment of high humidity, not only was the incidence of the digestive syndrome lowest, but the lessened incidence occurred in the smaller rather than the larger infants. The increase in the incidence in the groups weighing 5 pounds or more under high

TABLE 22.—*Relative Severity of "Digestive Syndromes" According to Body Weight and Relative Humidity*

	Unconditioned Nursery (1923-1925) Natural Humidity		Conditioned Nurseries (1926-1929)			
			Low Relative Humidity (25-49%)		High Relative Humidity (50-75%)	
Weight, Pounds	Total No. Infant-Weeks	Per Cent of Severity	Total No. Infant-Weeks	Per Cent of Severity	Total No. Infant-Weeks	Per Cent of Severity
1.5-1.9	0	....	6	16.7	3	0.0
2.0-2.4	1	....	8	12.5	14	7.1
2.5-2.9	19	47.3	29	37.9	45	2.2
3.0-3.4	43	18.6	23	17.4	109	8.3
3.5-3.9	89	12.4	18	11.1	174	5.7
4.0-4.4	106	17.9	37	18.9	176	8.0
4.5-4.9	103	18.4	32	15.6	168	7.1
5.0-5.4	84	8.3	25	4.0	86	12.8
5.5-5.9	67	11.9	10	30.0	39	10.3
6.0 and over	103	5.8	16	12.5	22	13.6
Average						
2.5-3.9	..	26.1	..	22.1	..	5.4
4.0-4.9	..	18.1	..	17.2	..	7.5
5.0 and over	..	8.7	..	15.5	..	12.2
Average of all weights	..	17.7	..	18.3	..	8.4

humidity is analogous to the situation with regard to gain in weight and growth in length. Thus it would appear, again, that in premature infants weighing 5 pounds or more, the temperature conditions under high humidity may have been the factor causing a higher incidence of the digestive syndrome because these temperature conditions exceeded the optimum requirements of the larger infants.

Table 22 gives the relative severity of the digestive syndrome. Here, severity takes account of the incidence and duration as well. The duration is expressed in infant-weeks. For instance, two infant-weeks of the syndrome may consist of a single incidence (a single case of two weeks' duration) or of two different cases, each lasting a week. The percentage severity in columns 3, 5 and 7 has been computed by dividing the number of infant-weeks of the syndrome in any given weight group by the corresponding total number of infant-weeks.

The general trend of severity of the syndrome is similar to that of incidence. It is minimum under high humidity and maximum under low humidity. The increase in severity in infants weighing 5 pounds and over under high humidity is presumably due to the same causes which were responsible for the increase in incidence, as previously mentioned.

Incidence and Severity Under Alternating Conditions of Humidity.—In comparing incidence and severity under high and low humidity (tables 21 and 22), exception may be taken to the fact that in the data for high humidity are included many infants who had not been exposed to low humidity. Moreover, both incidence and severity (tables 21 and 22) are not charged to the humidity in which the syndrome developed, but to the environmental conditions in which the symptoms were present regardless of where they developed. In order to guard against the possibility of drawing erroneous conclusions, table 23 was prepared. In this table are included infants who were under both high and low humidity during the period in which the humidity was alternated weekly or biweekly between high and low. Both incidence and severity in table 23 are arranged according to the humidity in which the syndrome developed. In other words, if an infant developed the digestive disturbance in low humidity and the disorder continued through the following week when the humidity was high, both incidence and severity (table 23) are charged to low humidity, whereas in tables 21 and 22, they are charged to both low and high humidity because the syndrome was present in both environments.

TABLE 23.—*Incidence and Severity of "Digestive Syndromes" Among a Comparable Group of Sixty-Three Infants Exposed to Alternating Humidity Conditions*

Relative Humidity	Number of Cases	Per Cent of Incidence	Infant-Weeks	Total No. of Infant-Weeks	Per Cent of Severity
Low (25-49%).....	19	30.2	41	202	20.3
High (50-75%).....	7	11.1	16	298	5.4

In sixty-two infants exposed to the alternating conditions of humidity, the digestive syndrome occurred in twenty-six. In nineteen patients it developed under low humidity. Six of these patients died. In the remaining seven cases, under high humidity, no fatalities resulted. It can be seen in table 23 that the incidence is about three times greater under low than under high humidity. Correspondingly, the severity of the digestive syndrome is reduced to one fourth under high humidity (column 6).

Undoubtedly, the incidence and severity under high humidity for infants weighing less than 5 pounds would have been considerably lower than that shown in tables 21 to 23 if high humidity had prevailed through the entire period of the study and studies of the response to

TABLE 24.—*Comparative Incidence and Severity of "Digestive Syndromes" Under Alternating and Under Continuously High Humidity* *

	Alternating Humidity (1926-1927)			Continuous High Humidity (1928-1929)		
Weight, Pounds	Total No. of Infants in Group	Per Cent of Incidence	Per Cent of Severity	Total No of Infants in Group	Per Cent of Incidence	Per Cent of Severity
Under 3.0	5	0.0	0.0	19	5.3	1.8
3.0-3.4	11	9.1	5.0	34	5.9	2.4
3.5-3.9	27	11.1	7.1	53	1.9	1.7
4.0-4.4	40	12.5	8.3	58	3.4	3.1
4.5-4.9	40	7.5	4.8	61	8.2	5.9
5.0-5.4	37	13.5	9.6	25	16.0	15.1
5.5-5.9	24	4.2	3.2	7	28.6	28.6
6.0 and over	15	20.0	13.6	..	....	....
Average under 5.0	..	8.0	5.0	..	4.9	3.0
Average over 5.0	..	12.6	8.8	..	22.3	21.8

* The relative humidity was from 50 to 75 per cent. Patients were excluded who showed signs of syndromes on admission.

TABLE 25.—*Weekly Relative Incidence of "Digestive Syndromes" According to Body Weight and Sex*

	Unconditioned Nursery (1923-1925) Natural Humidity				Conditioned Nurseries (1926-1929) High and Low Humidities Combined			
	Boys		Girls		Boys		Girls	
Weight, Pounds	Total No. of Infants in Group	Per Cent of Incidence	Total No. of Infants in Group	Per Cent of Incidence	Total No. of Infants in Group	Per Cent of Incidence	Total No. of Infants in Group	Per Cent of Incidence
1.5-1.9	0	....	0	....	0	....	3	33.3
2.0-2.4	0	....	1	....	4	25.0	6	16.7
2.5-2.9	3	66.7	8	25.0	13	30.8	19	21.1
3.0-3.4	14	21.4	12	25.0	22	13.6	33	15.2
3.5-3.9	25	24.0	19	21.1	40	12.5	48	8.3
4.0-4.4	29	24.2	20	15.0	53	17.0	58	10.3
4.5-4.9	32	25.0	23	21.7	59	11.9	58	8.6
5.0-5.4	28	7.1	23	17.4	41	12.1	32	12.5
5.5-5.9	21	19.1	18	16.7	24	29.2	14	0.0
6.0 and over	17	11.8	16	12.5	11	27.3	6	0.0
Average								
2.5-3.9	..	37.4	..	23.7	..	19.0	..	14.9
4.0-4.9	..	24.6	..	18.4	..	14.5	..	9.5
5.0 and over	..	12.7	..	15.5	..	22.9	..	4.2

low humidity had not been attempted. This statement holds true according to table 24, which shows data for 1928 to 1929 when a high relative humidity prevailed, and data for 1926 to 1927 when the humidity was alternated from high to low levels.

Sex in Relation to Digestive Syndromes.—In tables 25 and 26 are given the incidence and severity of the syndrome among boys and girls. Both incidence and severity are considerably lower in girls than in

boys of the same weight groups, being thereby analogous to the situation with regard to increase in weight, and, as will be shown, the mortality trend.

Age in Relation to First Incidence of Symptoms.—In table 27 the incidence of the important criteria is arranged according to the age after birth at which the symptoms first occurred. The per cent of incidence in column 3 was computed by dividing the number of cases in any given age group by the total number of infants in that group. It will be observed that the incidence was quite low during the first week of life, and increased rather abruptly in the second week. The maximum inci-

TABLE 26.—*Relative Severity of "Digestive Syndromes" According to Body Weight and Sex*

	Unconditioned Nursery (1923-1925) Natural Humidity				Conditioned Nurseries (1926-1929) High and Low Humidities Combined			
	Boys		Girls		Boys		Girls	
Weight, Pounds	Total No. of Infant-Weeks	Per Cent of Severity	Total No. of Infant-Weeks	Per Cent of Severity	Total No. of Infant-Weeks	Per Cent of Severity	Total No. of Infant-Weeks	Per Cent of Severity
1.5-1.9	0	....	0	....	0	....	9	11.1
2.0-2.4	0	....	1	....	9	11.1	13	7.7
2.5-2.9	4	75.0	15	40.0	39	20.5	35	11.4
3.0-3.4	23	21.8	20	15.0	54	9.3	78	10.3
3.5-3.9	53	11.3	36	13.9	92	7.6	100	5.0
4.0-4.4	63	19.1	43	16.3	104	12.5	109	7.3
4.5-4.9	59	22.0	44	13.6	95	11.6	105	5.7
5.0-5.4	42	4.8	42	11.9	63	12.7	48	8.3
5.5-5.9	38	13.2	29	10.3	32	21.8	17	0.0
6.0 and over	35	11.4	68	2.9	25	20.0	13	0.0
Average								
2.5-3.9	..	36.0	..	23.0	..	12.5	..	8.9
4.0-4.9	..	20.6	..	15.0	..	12.1	..	6.5
5.0 and over	..	9.8	..	8.4	..	18.2	..	2.8

dence occurred between the fifth and tenth week; by the eighteenth week the tendency had disappeared.

The data presented in this paper afford ample proof that clinical manifestations of disturbed bodily function are prone to develop in premature infants living in an environment of low humidity, particularly for a week or more at a time, whereas in a relatively high humidity, the incidence, severity and duration of the concomitant clinical symptoms are reduced.

While definite conclusions cannot be drawn as to the mechanism of action of changing environmental air conditions, from the information at hand it is apparent that humidity rather than temperature or air purity is the factor chiefly responsible for initiating symptoms referable to the gastro-intestinal system. In the studies which were conducted, the ventilation rate remained constant and the difference in temperature

under low and high humidities did not vary more than 3 F., in most instances. Also, in a number of very small infants who required a temperature as high as 90 F. in order to stabilize the body temperature, evidences of the digestive syndrome did not appear when the needed higher temperature was afforded in an open, heated bed and the babies were kept in an atmosphere with a relative humidity between 55 and 65 per cent.

Presumably the onset of the syndrome in premature infants who remained beyond the threshold period in an environment of low humidity is due to a disturbance of water metabolism brought about through the great loss of water from the skin and lungs. With a continuation of the

TABLE 27.—*Incidence of "Digestive Syndrome" in Relation to Chronological Age (1923-1929)*

Week of Life in Which Syndrome First Occurred	Number of Cases	Per Cent of Incidence
1	1	2.0
2	5	6.7
3	7	6.2
4	6	4.5
5	11	7.3
6	8	5.5
7	11	8.1
8	12	9.6
9	5	4.6
10	8	8.8
11	4	5.1
12	0	0.0
13	3	5.6
14	2	5.0
15	2	5.9
16	2	7.7
17	1	4.6
18	0	0.0
19	0	0.0
20	0	0.0

early signs—vomiting and diarrhea—further depletion of the body tissues through the excessive loss of water and essential substances may readily induce a critical state of dehydration. The resultant lowering of the resistance of the tissues opens the way for invasion of pathogenic organisms and the development of secondary infection—a most frequent cause for the high mortality in infants whose principal physiologic functions are not fully mature.

In this connection, as the maximum incidence of the digestive syndrome occurred from the fifth to the tenth week of life, it is pertinent to draw attention to the parallelism between the onset of the digestive symptoms according to the age in weeks and the state of physiologic function in premature infants who exhibit, as it were, a "physiologic lag" in comparison with the processes so perfectly adjusted at birth in the normal full-term infant.

A few of the physiologic peculiarities will be cited to illustrate this association. As found by Baty, Diamond and one of us (K. D. B.),[27] the hemoglobin index reaches its lowest level of between 30 and 50 per cent during the fifth to the tenth week. Hamilton[28] demonstrated that calcium poverty attains its maximum between the eighth and fifteenth week or about the time when the incidence of physiologic craniotabes as shown by Sisson and Ganz[29] is highest (from the eighth to the twentieth week). Utheim[30] reported a low amount of serum protein in the blood of premature infants at birth. It is conceivable, yet it cannot be stated positively, that these changes may to some extent be related to humidity and that the clinical manifestations may be but an expression of profound disturbances of mineral salts, of protein and of general metabolism. It is at least of passing interest to restate that Romanoff[25] believes that the influence of humidity is both physiologic and physical, as he found, in certain stages of development of the chick embryo, that calcium metabolism was somewhat hastened in high humidity and retarded in low humidity, an observation in all respects comparable to the response in growth of premature infants.

Treatment of the Digestive Syndrome.—With the full realization of the importance of low humidity as a factor contributing to the development of gastro-intestinal symptoms, the chief principles of therapy were directed toward changes in the diet and environment and the institution of transfusion. These measures proved most beneficial, provided they were instituted early and at the time of onset of any one or any combination of the "danger signals." The signs which we took as indicative of danger were lessening in activity, slowness in taking or refusal of food, regurgitation or vomiting, alteration in the character and increase in the number of stools and instability of the body temperature. Failure to gain or a loss in weight, as a rule, followed the onset of these minor symptoms. As stated previously, if these danger signals continued and were not corrected, an undesirable state of dehydration and secondary infection was prone to develop.

The routine plan of treatment was as follows: At the onset of the first signs of danger, the total caloric value of the food was reduced and,

27. Blackfan, K. D.; Baty, J. M., and Diamond, L. K.: The Anemias of Childhood, Oxford Monographs, New York, Oxford University Press, 1930, vol. 9, chap. 25.

28. Hamilton, Bengt: The Calcium and Phosphorus Metabolism of Prematurely Born Infants, Acta pædiat. **2:1**, 1922 (in English).

29. Sisson, W. R., and Ganz, R. N.: The Relation of Craniotabes in Premature Infants to Rickets, Tr. Am. Pediat. Soc. **39:**49, 1927.

30. Utheim, Kirsten: A Study of the Blood and Its Circulation in Normal Infants and in Infants Suffering from Chronic Nutritional Disturbances, Am. J. Dis. Child. **20:**366 (Nov.) 1920.

for a short time, protein milk was substituted at alternate feedings. Infants weighing less than 3 pounds were removed to the nursery where a relative humidity of 65 per cent was maintained regularly. Here, if necessary, for the purpose of stabilizing their body temperature, the infants were placed in an electric incubator, and the temperature was regulated according to their needs. The indirect method of transfusion was used for the injection of citrated whole blood intravenously.[31]

In the majority of instances the response to these measures was prompt, as shown by cessation of vomiting, infrequency of stools, a betterment in the general activity and stabilization of the body temperature. However, when immediate improvement did not follow, transfusion was repeated at daily or less frequent intervals.

We are well aware that criticism might be directed toward the frequency with which the premature infants in this series were given transfusions, but experience has shown, and the analyses of the mortality statistics reveal, that response to the injection of whole blood is much more permanent if the treatment is given, in the event of the absence of infection or congenital anomalies incompatible with life, at the onset of any one or any combination of the "danger signals" rather than after the development of more serious signs which are commonly taken as the indication for employing this procedure. Only in exceptional cases was it necessary to resort to the use of physiologic solution of sodium chloride and dextrose solution parenterally.

MORTALITY RATE IN UNCONDITIONED AND CONDITIONED NURSERIES [32]

From June, 1923, to January, 1926, one hundred and twenty-three premature infants were admitted to the unconditioned nursery of the Infants' Hospital. Of these, sixty-four died and fifty-nine were discharged to their homes. During the period from January, 1926, to December, 1929, inclusive, after the nurseries for premature infants had been conditioned mechanically, two hundred and twenty-nine infants

31. The technic did not differ from that employed in older children, with the exception that for entering the veins of the scalp, needles were used in which the caliber was so small that the blood did not flow through readily. The pressure necessary to force the volume of blood through the needle was afforded by using a 50 cc. syringe. The longitudinal sinus was practically never used. The amount of blood injected was about 10 cc. per pound of body weight. It has been the practice to determine the type and to cross-agglutinate the blood of the donor and the recipient. If further transfusions are indicated, the foregoing procedure is repeated, for, as is well recognized, the blood type, and therefore its agglutination reaction, becomes fixed during the first few months of life.

32. The term fatality rate has not been used in this report in order to avoid the assumption that the chief underlying cause of death is prematurity.

were admitted; of these, ninety-seven died and one hundred and thirty-two were discharged to their homes.

It should be made clear that the differences in the gross, crude and net death rates (table 28) from year to year or between the old and the new nurseries are not directly comparable because the mortality varies greatly with age, weight, sex and general conditions of the infants. Moreover, the infants were born outside the hospital and were therefore exposed to chilling and infection for a variable period at home and in transit to the hospital. They were often critically ill, and it was not

TABLE 28.—*Yearly Gross, Crude and Net Mortality of Premature Infants*

Years	(a) Number of Infants Admitted to Nurseries	(b) Total Number of Deaths	General Gross Death Rate $\frac{b \times 100}{a}$ per Cent	(c) Died Within 48 Hours After Admission	General Crude Death Rate $\frac{(b-c) \times 100}{(a-c)}$ per Cent	(d) Number of Unavoidable Deaths	General Net Death Rate $\frac{(b-c-d) \times 100}{(a-c-d)}$ per Cent
Unconditioned Nursery; No Mechanical Ventilation; Natural Humidity							
1923	17	13	76.5	6 (35.2%)	63.6	2 (11.8%)	55.5
1924	49	26	53.1	9 (18.4%)	42.5	6 (12.3%)	32.3
1925	57	25	43.8	12 (21.0%)	28.9	5 (8.6%)	20.0
Conditioned Nurseries; Study of Optimum Conditions; Humidity Alternating Between Low and High							
1926	54	22	40.7	11 (20.4%)	25.6	6 (11.1%)	13.5
1927	58	29	50.0	14 (24.2%)	34.1	11 (18.9%)	12.1
Conditioned Nurseries; Optimum Air Conditions Applied; Humidity Always High							
1928	56	18	32.1	7 (12.5%)	22.4	10 (17.9%)	2.6
1929	61	28	45.9	20 (32.8%)	19.5	8 (13.1%)	0.0

unusual for infants to succumb while being admitted. The general net death rate (table 28, column 8) allows to some extent for the latter variable conditions, but it does not take into consideration important variations in the biologic and physical characteristics of the infants, fetal age and weight at birth and weight on admission. The net or revised rate was computed by excluding (*a*) all deaths occurring within forty-eight hours of admission, (*b*) deaths due to congenital malformations incompatible with life and (*c*) deaths due to acute and chronic infections present at the time of admission. The last two causes of death were grouped together and are referred to as "unavoidable deaths" in column 7, table 28.

Without resorting to a more elaborate distinction of the different group of infants according to physical characteristics and causes of

death, as related to optimum air conditions, it would be difficult to determine the proportionate part which improved medical methods and nursing care and the application of air conditioning have played in the decrease of the general death rate. A possible reason for the absence of a striking change of the mortality trend during 1926 may be that during the first two years of operation of the new system, the conditions in the nurseries were being changed weekly over a wide range for the purpose of determining the optimum temperature, humidity and ventilation rate. The rather sharp reduction in death rate from 1928 (column 8, table 28) is indicative of the direct effect of an environment in which the optimum air conditions were maintained with regularity.

However, with this reduction in the general net mortality, a definite change did not take place in the death rate of infants dying within forty-eight hours after admission (column 5) or in the percentage of unavoidable deaths (column 7). This would seem to indicate that any further improvement in the gross death rate must be sought for in the conditions affecting the infants prior to their entry to the hospital, and especially in the causes of the deaths which occur within the first few days of life.[33] As it was known that exposure of the infants during transportation to the hospital might be an important factor in the death of the infants, a small hand ambulance equipped with an electric heating element which could be attached to the battery system of an automobile was procured in 1927. Whenever possible, a hospital attendant was sent with the ambulance to bring the infant to the institution. According to table 28, columns 5 and 7, however, neither the percentage of deaths occurring within forty-eight hours nor the percentage of "unavoidable deaths" appears to have been affected by the introduction of the heated ambulance.

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33. Recent studies by Dr. Stewart H. Clifford (Studies on Reduction of Neonatal Mortality, papers nos. I, II and III, to be published) at the Boston Lying-In Hospital suggest a possible relationship between the mortality rate of premature infants during the first few days of life and the mode of delivery. In comparable weight groups the mortality for premature infants delivered by cesarean section was 44.4 per cent; for deliveries by breech extraction, 42 per cent; for normal deliveries, 25.7 per cent, and for low forceps deliveries, 18 per cent. The investigation has revealed that the life or death of the premature infant is related directly to the use or nonuse of morphine prior to delivery and to the type of anesthesia employed at the time of delivery. Furthermore, with the aid of a modified roentgenologic technic, it has been possible to estimate with a high degree of accuracy the actual weight of the fetus in utero, and thus by following the growth curve in utero, a prediction may be made as to the time of delivering a viable infant with the best chances for growth, if for maternal causes delivery is indicated. The conclusion is drawn that these factors—weight of the fetus at birth, drugs and method of delivery—undoubtedly play an important part in the high mortality among premature infants, especially in the first few days of life.

Mortality in Relation to Weight and Age on Admission.—Table 29 gives the gross and net mortality in the unconditioned and conditioned nurseries according to weight on admission. It is interesting to notice the increased number of patients in the three lowest weight groups from 1926 to 1929 as compared with 1923 to 1925. In this earlier period no infants were admitted with a weight less than 2 pounds, whereas in the later four year period, fifteen infants approaching this weight entered. Sixty-one patients weighing between 2 and 3 pounds were admitted in the period from 1926 to 1929, whereas there were twenty-two such cases from 1923 to 1925. The age at admission to the unconditioned and conditioned nurseries differed in a similar manner.

TABLE 29.—*Mortality According to Weight on Admission*

Weight on Admission, Pounds	Unconditioned Nursery (1923-1925)				Conditioned Nurseries (1926-1929)			
	Number of Cases	Per Cent of Total Admissions	Number of Deaths	Per Cent of Mortality	Number of Cases	Per Cent of Total Admissions	Number of Deaths	Per Cent of Mortality
Gross Mortality (All Infants)								
1.5-1.9	0	0.0	..	....	15	6.6	12	80.0
2.0-2.4	5	4.1	5	100.0	20	8.7	15	75.0
2.5-2.9	17	13.8	14	82.3	41	17.9	20	48.8
3.0-3.4	28	22.7	12	42.9	35	15.3	13	37.1
3.5-3.9	24	19.5	11	45.8	44	19.2	14	31.8
4.0-4.4	17	13.8	7	41.2	37	16.2	9	24.3
4.5 and over	27	22.0	10	37.0	33	14.4	10	30.3
Unknown	5	4.1	5	100.0	4	1.7	4	100.0
Net Mortality (Unavoidable and 48 Hour Deaths Excluded)								
1.5-1.9	0	0.0	..	....	3	2.1	0	0.0
2.0-2.4	1	1.2	1	100.0	5	3.5	0	0.0
2.5-2.9	8	9.6	5	62.5	24	16.9	3	12.5
3.0-3.4	21	25.3	5	23.8	23	16.2	1	4.3
3.5-3.9	20	24.2	7	35.0	32	22.6	2	6.3
4.0-4.4	13	15.6	3	23.1	30	21.1	2	6.7
4.5 and over	20	24.1	3	15.0	25	17.6	2	8.0
All weights	83	100.0	24	28.9	142	100.0	10	7.0

In the former nursery it ranged uniformly within the four age groups shown in table 30. In other words, there were about as many infants in the group admitted at an age of 2 days or less as there were in any other age group. In the conditioned nurseries, on the other hand, 40 per cent of the infants were less than 2 days old on admission, 30 per cent between 3 and 15 days old, 19 per cent between 16 and 30 days old and 11 per cent more than a month old.

It will be seen in tables 29 and 30 that the gross death rate varies inversely with the weight and age on admission, being in all instances lower in the conditioned nurseries than in the unconditioned nursery. A significant lowering of the mortality can be observed in infants of the low weight group. The reduction in the gross mortality rate ranges from about 29 per cent among the two lowest weight groups to about 12 per cent in the two highest weight groups. In the net mortality, the reduction is much greater in weight groups under 4 pounds, the rate

in the conditioned nurseries being less than one sixth of that in the unconditioned nursery. The general net mortality for all weight and age groups (bottom of tables 29 and 30) was 7 per cent in the conditioned nurseries as compared with 28.9 per cent in the unconditioned nursery.

For infants weighing 4½ pounds and over on admission, the upward trend in mortality rate in the conditioned nurseries is real. It has been due to a special group of immature infants born between the fetal ages of seven and a half and nine months, with a weight at birth of nearly 4½ pounds or more, of mothers with intercurrent diseases during pregnancy.

As indicated in table 29, the maximum reduction in the net mortality during 1926 to 1929 occurred among infants of the lower weight groups.

TABLE 30.—*Mortality According to Chronological Age on Admission*

Age on Admission, Days	Unconditioned Nursery (1923-1925)				Conditioned Nurseries (1926-1929)			
	Number of Cases Admitted	Per Cent of Total Admissions	Number of Deaths	Per Cent of Mortality	Number of Cases Admitted	Per Cent of Total Admissions	Number of Deaths	Per Cent of Mortality
Gross Mortality (All Infants)								
2 or less	32	26.0	26	81.2	92	40.2	58	63.0
3 to 15	29	23.6	13	44.8	69	30.1	21	30.4
16 to 30	34	27.7	15	44.1	43	18.8	13	30.2
31 and over	28	22.7	10	35.7	25	10.9	5	20.0
Net Mortality (Unavoidable and 48 Hour Deaths Excluded)								
2 or less	11	13.3	5	45.5	37	26.1	3	8.1
3 to 15	22	26.5	6	27.3	52	36.6	4	7.7
16 to 30	28	33.7	9	32.1	33	23.2	3	9.1
31 and over	22	26.5	4	18.2	20	14.1	0	0.0
All ages	83	100.0	24	28.9	142	100.0	10	7.0

As the number of infants was considerably larger in the new nurseries than in the old one, this difference in the total number of cases must be considered in comparing the general mortality rates in table 28 either from year to year, or between the unconditioned and the conditioned nurseries.

In the unconditioned nursery, both the net and the gross mortality rates vary inversely with the weight and age on admission. The net mortality in the conditioned nurseries apparently does not depend entirely on the weight and age on admission (tables 29 and 30). Even when the mortality rates are classified according to weight and age on admission, as in table 31, the variation in the unconditioned nursery still persists in an inverse proportion to the age, for any given weight group, or to the weight for any given age group. In the conditioned nurseries, the inverse weight-mortality relationship appears to hold only for infants of 2 days or less of age. In all of the other age groups the variation is irregular.

Mortality According to Weight-Length Ratio.—When the number of deaths in the conditioned nurseries are arranged according to the weight-length ratio on admission, the gross mortality rate remains practically unaffected and the net death rate varies in an irregular manner, as shown in table 32. In other words, the weight-length ratio does not appear to be an important factor in the prognosis of the premature

TABLE 31.—*Mortality According to Weight and Age on Admission*

Weight on Admission, Pounds	Unconditioned Nursery (1923-1925) Per Cent of Mortality			Conditioned Nurseries (1926-1929) Per Cent of Mortality		
	2 Days Old or Less	3 to 30 Days Old	31 Days or Older	Under 2 Days Old	3 to 30 Days Old	31 Days or Older
Gross Mortality (All Infants)						
Under 3	100.0	85.7	60.0	80.0	21.7	66.7
3 to 4	69.2	41.2	0.0	52.2	26.0	33.3
Over 4	60.0	33.3	38.9	31.6	36.1	0.0
Unknown	100.0	100.0	.....	.....	100.0	100.0
All weights	81.1	44.4	35.7	63.1	30.4	20.0
Net Mortality (Unavoidable and 48 Hour Deaths Excluded)						
Under 3	100.0	66.7	50.0	16.7	5.3	0.0
3 to 4	33.3	33.3	0.0	8.3	5.1	0.0
Over 4	33.3	17.7	15.4	0.0	14.8	0.0
Unknown	.. ..	.....	.....	.....	.....	.....
All weights	45.5	30.0	18.2	8.1	8.2	0.0

TABLE 32.—*Mortality According to Weight-Length Ratio on Admission (All Infants, 1926-1929)*

Weight-Length Ratio, Pounds per Inch	Gross Mortality			Net Mortality		
	No. of Cases	No. of Deaths	Per Cent of Mortality	No. of Cases	No. of Deaths	Per Cent of Mortality
Under 0.150	13	7	53.8	7	1	15.7
0.150-0.174	20	6	30.0	14	0	0.0
0.175-0.199	33	11	33.3	22	0	0.0
0.200-0.224	31	7	22.6	25	1	4.0
0.225-0.249	43	14	32.6	34	5	14.7
0.250 and up	17	6	35.3	12	1	8.3
Unknown	72	46	63.9	28	2	7.1
All ratios	229	97	42.3	142	10	7.0

infant, which is analogous to the situation with regard to stabilization of body temperature and increases in body weight and length.

Mortality in Relation to Fetal Age and Birth Weight.[34]—As indicated in tables 33 and 34, in the mortality rate according to the approximate fetal age and birth weight, practically the same differences between the unconditioned and conditioned nurseries occur as were found on the basis of weight and age on admission (tables 29 and 30). Neither the fetal age nor the natal weight, however, is as sensitive an index of gross mortality as the weight on admission (table 29), but

34. The limitations of the data under this title have been mentioned previously in footnote 19.

the natal weight appears to be a safer prognostic index than the fetal age. This is in agreement with conclusions reached by Cook,[22] Capper [35] and others. In the unconditioned nursery, the net mortality bears but little relation to fetal age or weight at birth, and in the conditioned nurseries it bears no relation whatsoever (tables 33 and 34).

TABLE 33.—*Mortality According to Fetal Age*

Fetal Age, Months	Unconditioned Nursery (1923-1925)			Conditioned Nurseries (1926-1929)		
	No. of Admissions	No. of Deaths	Per Cent of Mortality	No. of Admissions	No. of Deaths	Per Cent of Mortality
	Gross Mortality (All Infants)					
6 and under	7	5	71.4	17	10	58.8
6½	6	3	50.0	21	12	57.1
7	49	28	57.2	66	29	43.9
7½	13	7	53.8	33	14	42.4
8-9	34	13	38.2	74	23	31.1
Unknown	14	8	57.1	18	9	50.0
	Net Mortality (Unavoidable and 48 Hour Deaths Excluded)					
6 and under	3	1	33.3	7	0	0.0
6½	4	1	25.0	10	1	10.0
7	33	12	36.4	40	3	7.5
7½	9	3	33.3	23	4	17.4
8-9	25	4	16.0	53	2	3.8
Unknown	9	3	33.3	9	0	0.0

TABLE 34.—*Mortality According to Weight at Birth*

Weight at Birth, Pounds	Unconditioned Nursery (1923-1925)			Conditioned Nurseries (1926-1929)		
	No. of Admissions	No. of Deaths	Per Cent of Mortality	No. of Admissions	No. of Deaths	Per Cent of Mortality
	Gross Mortality (All Infants)					
1.5-2.4	8	5	62.5	30	24	80.0
2.5-3.4	25	17	68.0	62	27	43.5
3.5-4.4	34	18	52.9	52	17	32.7
4.5 and over	24	11	45.8	45	17	37.8
Unknown	32	13	40.6	40	12	30.0
	Net Mortality (Unavoidable and 48 Hour Deaths Excluded)					
1.5-2.4	4	1	25.0	6	0	0.0
2.5-3.4	14	6	42.8	39	4	10.3
3.5-4.4	25	9	36.0	37	2	5.4
4.5 and over	16	3	18.8	31	3	9.7
Unknown	24	5	20.8	29	1	3.4

When the deaths in the different fetal-age groups are arranged according to birth weight, as in table 35, no significant relationship can be found. This may be due partly to the fact that the data do not deal with the mortality of premature infants who received institutional care from birth, but of infants who presumably have been subjected to chilling and exposure and to infection together with inadequate care from the time of birth. These unfavorable conditions cannot, of course, affect the fetal age, the weight at birth or the length on admission to

35. Capper, Aaron: The Fate and Development of the Immature and of the Premature Child, Am. J. Dis. Child. **35**:443 (March) 1928.

any appreciable extent, but they find a powerful reflection in the weight on admission, which in turn is related more to the weight at birth than to the fetal age. The difficulty in obtaining accurate data concerning the fetal age and the weight at birth may detract to some extent from their value as prognostic indexes.

Mortality According to Sex.—In table 36, the deaths in both the unconditioned and the conditioned nurseries were combined according

TABLE 35.—*Mortality According to Fetal Age and Weight at Birth*

Fetal, Age Months	Unconditioned Nursery (1923-1925) Per Cent of Mortality				Conditioned Nurseries (1926-1929) Per Cent of Mortality			
	Under 3 Pounds	3-4.4 Pounds	4.5 Pounds and Over	Unknown Weight	Under 3 Pounds	3-4.4 Pounds	4.5 Pounds and Over	Unknown Weight
Gross Mortality (All Infants)								
Under 7	66.7	60.0	....	50.0	72.0	33.3	100.0	0.0
7-8	66.7	60.7	60.0	44.4	75.0	29.3	40.0	26.7
8-9	100.0	41.7	33.3	25.0	16.7	34.5	30.4	31.2
Unknown	50.0	66.7	50.0	50.0	66.7	33.3	50.0	50.0
All ages	68.7	56.9	45.8	40.6	67.8	31.7	37.8	30.0
Net Mortality (Unavoidable and 48 Hour Deaths Excluded)								
Under 7	33.3	33.3	....	0.0	0.0	14.3	....	0.0
7-8	60.0	35.3	42.9	23.1	12.5	9.4	18.2	8.3
8-9	....	22.2	0.0	25.0	0.0	5.0	5.9	0.0
Unknown	0.0	60.0	0.0	0.0	0.0	0.0	0.0	0.0
All ages	44.4	35.3	18.8	20.8	4.8	8.2	9.7	3.4

TABLE 36.—*Mortality-Sex Ratio; Consolidated Data of Old and New Nurseries*

Weight on Admission, Pounds	Boys		Girls		Mortality-Sex Ratio
	Number of Cases	Per Cent of Mortality	Number of Cases	Per Cent of Mortality	
Gross Mortality (All Infants)					
Under 3 and unknown.....	40	72.5	67	68.6	106
3-4.....	73	43.8	58	31.0	141
Over 4.....	67	32.8	47	29.8	110
Net Mortality (Unavoidable and 48 Hour Deaths Excluded)					
Under 3.....	14	21.4	27	22.2	97
3-4.....	51	19.6	45	11.1	176
Over 4.....	53	15.1	35	5.7	264

to sex and arranged according to weight on admission. The death rate among boys is considerably higher than that among girls. The mortality-sex ratio in column 6 expresses the number of deaths in boys to a hundred deaths in girls. It was computed by dividing the death rate for boys by that for girls, and multiplying the ratio by one hundred. The great variation in the mortality-sex ratio is to be expected, but the data clearly show the importance of sex and weight in mortality studies. If the gross death rate were computed according to sex alone, regardless of body weight, the mortality among the sexes would be about equal. Statistically, this is an illusion that results from mass averages.

Bakwin's [36] study of the sex factor in general infantile mortality shows a sex ratio of 140 for the first three months of life, decreasing progressively after that. The gross mortality sex-ratio in this series is lower than that of Bakwin, while the net ratio is higher.

PRINCIPAL CONTRIBUTORY CAUSES OF DEATH

For the purpose of studying the mortality rate in its relation to the principal contributory cause of death, the data are listed under four main headings according to the cause as determined by necropsy in eighty-one of the one hundred and sixty-one patients and according to the clinical diagnosis in the remaining patients. An arbitrary classification [37] which has been used is as follows: (*a*) infection, acute and chronic; (*b*) congenital anomalies; (*c*) hemorrhage (petechial or gross intracranial), and (*d*) unclassified.

In table 37, the frequencies of the contributory causes of death are arranged according to the fetal age in months so far as it could be estimated, the presumable weight at birth, the actual weight and age at admission and the weight and age at the time of death. These data are given so that a more clear distinction may be made between the results obtained in the unconditioned nursery (1923 to 1925) and those obtained in the conditioned nurseries (1926 to 1929).

In the unclassified group there were forty-nine cases in the total number of fatalities in which the contributory cause of death could not be determined with such certainty as to warrant the cases being included in any one of the other three groups. The outstanding clinical signs in this group were cyanosis, irregularities of respiration and extreme instability of the body temperature. With the information afforded by physical examination and laboratory evidence, it was not possible to differentiate between such underlying pathologic conditions as immaturity of the vital processes, atelectasis, infection, hemorrhage and congenital anomalies. Five infants died in the admission room, nineteen within two days and fourteen within fifteen days, and the remaining patients died shortly thereafter.

There were seventeen patients afflicted with congenital anomalies incompatible with life. The developmental abnormalities involved practically all of the regional systems of the body either singly or in combination—the brain and spinal cord, the respiratory and cardiovascular

36. Bakwin, Harry: The Sex Factor in Infant Mortality, Human Biol. **1**:90, 1929.

37. Dr. Sidney Farber assisted in classifying the various causes of death in this series of cases. It is intended, in a subsequent report from this clinic, to describe in more detail the specific pathologic changes in premature infants, at which time the questions concerning atelectasis and asphyxia will be discussed.

TABLE 37.—*Contributory Causes of Death in Relation to Birth, Admission and Death Statistics*

	Unconditioned Nursery (1923-1925)						Conditioned Nurseries (1926-1929)					
	Acute and Chronic Infections	Congenital Deformities	Hemorrhage: Multiple Petechial	Hemorrhage: Intracranial	Unclassified	Total	Acute and Chronic Infections	Congenital Deformities	Hemorrhage: Multiple Petechial	Hemorrhage: Intracranial	Unclassified	Total
Total number of cases	45	3	1	1	14	64	31	14	10	7	35	97
Fetal age, months												
Under 7	4	..	..	..	4	8	7	2	4	3	6	22
7-8	26	2	1	..	6	35	12	4	4	3	20	43
8-9	12	..	..	..	1	13	10	8	..	1	4	23
Unknown	3	1	..	1	3	8	2	..	2	..	5	9
Weight at birth, pounds												
1.5-2.4	2	..	..	..	3	5	5	4	3	1	11	24
2.5-3.4	12	1	1	..	3	17	10	..	4	4	9	27
3.5-4.4	15	1	..	..	2	18	6	6	..	2	3	17
4.5 and over	8	..	..	..	3	11	7	3	3	..	4	17
Unknown	8	1	..	1	3	13	3	1	..	..	8	12
Weight on admission, pounds												
1.5-2.4	3	..	..	..	2	5	7	4	3	1	12	27
2.5-3.4	16	2	1	..	7	26	10	2	4	5	12	33
3.5-4.4	17	..	..	..	1	18	11	6	1	1	4	23
4.5 and over	7	1	..	..	2	10	3	1	2	..	4	10
Unknown	2	..	..	1	2	5	..	1	..	..	3	4
Age on admission, days												
2 or less	14	..	1	1	10	26	15	5	10	6	22	58
3-15	11	..	..	..	2	13	9	6	..	..	6	21
16-30	14	1	..	..	..	15	6	2	..	1	4	13
31 and over	6	2	..	..	2	10	1	1	..	..	3	5
Weight at death, pounds												
1.5-2.4	3	..	..	..	2	5	8	4	3	1	14	30
2.5-3.4	18	2	1	..	7	28	9	1	4	5	11	30
3.5-4.4	16	1	..	..	1	18	9	5	1	1	4	20
4.5 and over	6	..	..	..	2	8	5	3	2	..	3	13
Unknown	2	..	..	1	2	5	..	1	..	..	3	4
Age at death, days												
2 or less	4	..	1	1	9	15	6	3	9	5	15	38
3-15	9	..	..	..	3	12	7	2	1	1	11	22
16-30	12	..	..	..	..	12	8	2	..	..	4	14
31 and over	20	3	..	..	2	25	10	7	..	1	5	23

systems and the alimentary and genito-urinary tracts. It can be seen that there was a notable increase in the number of deaths of such patients in the air-conditioned nursery, resulting in all probability from the admission of larger numbers of such patients after the nursery had been equipped especially to care for congenitally diseased and malformed infants. As might be expected, the estimated fetal age, the weight on admission and the duration of life showed extreme variations.

In nineteen patients, necropsy revealed microscopic and macroscopic evidences of hemorrhage in the brain, spinal cord, respiratory, alimentary or genito-urinary tracts, liver or suprarenal glands. Multiple petechial hemorrhages which were found in eleven cases occurred almost exclusively in patients with an estimated fetal age of less than 8 months and with comparatively low weights on admission. Ten patients died within the first two days of life, and the one remaining patient at the end of two weeks.

In the eight patients with intracranial hemorrhage, the estimated fetal age was from 6 to 7 months in all but one, and in six patients the weight on admission was less than 3½ pounds. The duration of life in six patients was less than twenty-four hours; one patient lived four days, and the remaining patient died thirty-four days after birth. It is not justifiable to conclude that the hemorrhages found microscopically were sufficient to cause death in every case, but in nineteen patients the hemorrhage undoubtedly was the causative factor.

Turning now to the question of either acute or chronic infection as the principal contributory cause of death, simple computation (table 37) will show that this cause accounted for 70.3 per cent of the total number of deaths in the unconditioned nursery and for 31.9 per cent of the deaths in the conditioned nurseries. Although reasonable precautions were taken to exclude from the nurseries patients with clinical signs of infections, it is at least possible that a relatively small number may have been so afflicted at the time of admission. While the respiratory system was chiefly involved, other less frequent sites were the gastro-intestinal and genito-urinary symptoms. Syphilis, septicemia, erysipelas and thrush were infrequently seen. The incidence of infection was only slightly related to the fetal age and body weight but was chiefly related to the relative humidity of the nurseries.

In table 38 is shown the net mortality in the conditioned nurseries compared with the principal contributory causes of death under low and high humidity. The deaths are grouped according to the humidity in which the derangement of bodily function began. In most instances both onset and death occurred in low humidity, though in two patients death occurred a few days after changing to high humidity.

Of the ten deaths in the air-conditioned nurseries, nine apparently were precipitated by low humidity, and only one by high humidity. Six of the nine patients affected by low humidity died of infection. The contributory cause of death was not determined in three patients. The single death in high humidity occurred in a patient with congenital malformations. According to table 38, the general net mortality rate from infection was 26.5 per cent in the old nursery, as compared with 9.7 in the new nurseries under low humidity, and with 0 under high humidity. The corresponding net mortality rates from all causes were 28.9 per cent in the unconditioned nursery, 14.5 per cent under low humidity and 0.7 per cent under high humidity.

The deaths of nine patients in this series took place during the period (1926 to 1927) when the relative humidity was being alternated

TABLE 38.—*Net Mortality According to Humidity* *

	Unconditioned Nursery (1923-1925) Natural Humidity		Conditioned Nurseries (1926-1929) Low Relative Humidity (25-49%)		High Relative Humidity (50-75%)	
Cause of Death	Number of Deaths	Per Cent of Admissions†	Number of Deaths	Per Cent of Cases Exposed‡	Number of Deaths	Per Cent of Cases Exposed§
Acute and chronic infections	22	26.5	6	9.7	0	0.0
Congenital deformities	1	1.2	0	0.0	1	0.7
Unclassified	1	1.2	3	4.8	0	0.0
All causes	24	28.9	9	14.5	1	0.7

* "Unavoidable" and forty-eight hour deaths were excluded.
† Number of admissions, 83.
‡ Number of infants exposed, 62.
§ Number of infants exposed, 139.

weekly, biweekly or triweekly, from low to high, for the purpose of determining the optimum humidity. The stormy course in these patients began from one to fifteen days after changing to the low humidity. In three patients the onset occurred at an age of from 2 to 3 weeks, in three patients around the fourth to fifth week of life and in the remaining three patients at from 6 to 8 weeks of age. Six infants died within a week after the onset of the digestive syndrome, and the remaining three patients from two to four weeks after the onset.

In 71 per cent of the "unavoidable" deaths from all causes, the downward course started in low humidity, as compared with 29 per cent of the cases in which it occurred in high humidity. These deaths were excluded from table 38 in order to eliminate the element of chance as much as possible.

Improvements in medical treatment and nursing care necessarily are factors to be considered in comparing the mortality rate in the conditioned nurseries under low humidity with that in the unconditioned nursery under natural humidity (table 38). However, the factors of

medical and nursing care cannot account for the striking reduction in the death rate under high humidity as compared with low humidity, because the medical and nursing plan was comparable throughout the period from 1926 to 1929. As a matter of fact, the infants were watched with greater attention during the periods of low humidity than during those of high humidity.

As the infant-weeks of exposure under high humidity were four times greater than under low humidity, the possibility of "chance" variations as an explanation of the lessened incidence in physiologic disturbances and deaths in high humidity may be dismissed from consideration. The mechanism of action and the nature of the injury produced by low humidity remain unknown, but the end-results seem quite clear.

GENERAL SUMMARY

The effect of environment on the growth and development of premature infants has been the subject of an investigation extending over a period of seven years. By means of a central air-conditioning system, the temperature, humidity and ventilation of the nurseries was kept automatically under control within the desired range. A technical description of the air-conditioning system is presented.

In order to reduce to a minimum those influences which would interfere with the drawing of valid conclusions, special consideration was given to keeping uniform such variables as type of subject, hygiene and clothing, nutriment and medical and nursing care. For the purpose of securing data with which to contrast the results of the study in the conditioned nurseries, an analysis was made of the hospital records of infants treated over a period of three years in the old unconditioned nursery, before the installation of the air-conditioning apparatus.

From the data presented, we feel justified in submitting the following conclusions:

1. The heat-regulatory mechanism in normal full-term infants was adequate to protect them from excessive heat by vasomotor shifts of the blood to the peripheral vessels and by ample secretion of sweat. Perspiration began when the difference in temperature between the skin and the rectum was from 2.8 to 4.5 F. In a cold environment, the regulation of body temperature, brought about by vasomotor shifts of blood to the internal organs by crying and restlessness, was equally effective. In premature infants, however, the physiologic response to, and the time of recovery from, the effects of heat and cold were related directly to the fetal age and body weight. In infants weighing between 4 and 5½ pounds, the protective responses were less marked than in full-term infants and the differences in temperature between the cheek and the rectum when sweating began varied between 0.8 and 4.2 F. In

small infants weighing between 1½ and 4 pounds, visible perspiration did not commence until the difference in temperature between the cheek and the rectum approached 1 F. The smaller infants perspired but slightly or not at all, and the rectal temperature rose considerably on exposure to heat. On exposure to cold, they likewise showed an imperfect defensive reaction.

2. The humidity best suited to stabilizing the body temperature of premature infants appears to be about 65 per cent, with a temperature ranging from 75 to 100 F., depending to some extent on the general constitutional state of the infant and the body weight. A humidity of 30 per cent induced instability of body temperature and other untoward effects often leading to serious consequences.

3. The body temperature of the premature infant can be controlled much more regularly in rooms in which the temperature, humidity and ventilation rate are adequately controlled than in rooms in which these physical factors are allowed to fluctuate.

4. Body temperature and fluctuations in body temperature under controlled air conditions are related to body weight. In low weight groups the body temperature was about 98 F. and the fluctuation comparatively high. As the weight increased, the body temperature rose, and the fluctuation was reduced until at about 5 pounds the temperature was stabilized close to 98.6 F. with a diurnal fluctuation of about 2 F. Thereafter the response of premature infants to the environment was similar to that of full-term infants. A subnormal temperature, particularly in the low weight groups, is a characteristic of prematurity. Attempts to raise the body temperature of small infants to the supposedly normal level of 98.6 F. are not necessary, as overheating may be detrimental to proper growth and even may lead to death.

5. The period of time over which the initial loss of weight continued averaged four and six-tenths days in the unconditioned nursery, four and two-tenths days in the conditioned nurseries under low humidity and three days under high humidity. The maximum initial loss of weight, 12.4 per cent, occurred among patients in the unconditioned nursery and the minimum initial loss in weight, 6 per cent, occurred in patients living in the conditioned nurseries under relatively high humidity. Under low humidity, the initial loss in weight was intermediate between these two figures. In the unconditioned nursery, the infants regained their weight at birth in an average of twenty-six and five-tenths days; in the conditioned nurseries, in an average of nineteen and five-tenths days under low humidity and fifteen and five-tenths days under high humidity. The period and the degree of initial loss in weight, as well as the time required to regain the weight at birth, varied in an inverse proportion to the weight at birth.

6. The maximum gain in weight in patients weighing less than 5 pounds occurred under hign humidity in the conditioned nurseries. The gain in weight was less under low humidity and in the unconditioned nursery. The least gain in weight occurred after removal to the general wards.

7. Whereas infants who weighed less than 4½ pounds gained more rapidly in high than in low humidity, the reverse was true of infants who weighed 4½ pounds or over.

8. The maximum rate of growth in length took place during the first and second month. The growth in length showed a closer association with the body weight than with any of the other physical factors studied. The growth of length was irregular when classified according to the age on admission, the actual length on admission and the fetal age. No difference was found between the growth of length of boys and of girls. High humidity exerted a favorable influence on the growth in length in infants weighing less than 5 pounds, but as was the case with gain in weight there was a greater increase in length under low humidity in infants weighing more than 5 pounds.

9. The length of residence in the conditioned nurseries depended largely on the weight at the time of admission, decreasing progressively with increasing weights on admission and being on an average 18 per cent less in the conditioned than in the unconditioned nurseries.

10. Air conditions in general and low humidity in particular exerted a conspicuous influence in initiating symptoms referable to the digestive tract. The incidence, as estimated according to an arbitrary index, was at a minimum when the humidity was high and at a maximum when the humidity was low. The highest incidence occurred in the low weight groups of infants living in the unconditioned nurseries and in the conditioned nursery under low humidity. Reversely, the lowest incidence under high humidity occurred in premature infants weighing less than 5 pounds. The increase in incidence under high humidity in the group weighing more than 5 pounds was analogous to the situation with regard to gain in weight and growth in length. The incidence of the disturbance referable to the digestive tract was about three times greater under low than under high humidity, while the duration was four times greater. It is of interest that the incidence and severity were considerably lower in girls than in boys of similar weight groups. The data herein presented afford ample proof that when premature infants live in an environment of low humidity, particularly for a week or more at a time, clinical manifestations of disturbed bodily function are prone to develop, whereas in a relatively high humidity the incidence, severity and duration of the concomitant symptoms are reduced.

11. The mortality rate varied according to weight, age, sex and general constitutional state of the infants. The gross death rate varied inversely as the weight and age on admission, being in all instances lower in the conditioned nurseries than in the unconditioned nursery. The most significant lowering of the gross mortality was observed in infants of the lowest weight groups. The reduction ranged from about 29 per cent among the two lowest weight groups to about 12 per cent in the two highest weight groups.

The reduction in the net mortality [38] was much greater in groups weighing less than 4 pounds, the rate in the conditioned nurseries being about one sixth of that in the unconditioned nursery. The general net mortality for all weight and age groups was 7 per cent in the conditioned nurseries as compared with 28.9 per cent in the unconditioned nursery.

With respect to relative humidity, the net mortality rate from all causes of death was 28.9 per cent in the unconditioned nursery, and in the conditioned nurseries under low and high humidity it was respectively, 14.9 and 0.7 per cent.

From this study it seemed clear that any further improvement in gross death rate must be sought for in the conditions affecting premature infants prior to their entry to the hospital, and especially in the causes of deaths which occur within the first few days of life. In premature infants the death rate among boys was considerably higher than that among girls.

12. Acute and chronic infections accounted for 70.3 per cent of the total number of deaths in the unconditioned nursery and for 31.9 per cent of the deaths in the conditioned nurseries. The general net mortality rate from infection was 26.5 per cent of the number of infants in the unconditioned nursery as compared with 9.7 per cent of those who lived in the conditioned nurseries under low humidity and 0 per cent under high humidity. In most instances, both the onset of the downward course and death occurred in low humidity, though in a few patients death occurred a few days after changing to high humidity.

13. Improved methods in the general medical and nursing care of premature infants, adopted as a direct consequence of this investigation, must be taken into consideration when the reduction in mortality in the conditioned nurseries under low humidity is contrasted with that in the unconditioned nursery under natural humidity. But these factors do not entirely account for the remarkable reduction in the death rate in the conditioned nurseries under high humidity as compared with the death rate under low humidity, as the same medical and nursing procedures were followed during the period over which the effects of high and low humidity were studied.

38. For definition see table 28.

14. The body weight is the most important single criterion for judging the environmental requirements of premature infants. This index has been found to be more reliable than the estimated fetal age, chronological age or body length.

15. In the light of the present study, the importance of optimum temperature, humidity and ventilation conditions in the growth and development of premature infants is demonstrable.